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The Beattie-Smith Lectures.[1]

(University of Melbourne.)

LECTURE I: RESEARCH IN PSYCHIATRY.

By JOHN F. J. CADE,

Medical Superintendent, Repatriation Mental Hospital, Bundoora, Victoria.

PSYCHIATRY has come a long way since Beattie-Smith lectured upon the subject to final-year medical students at the end of last century. He is only a name to me, but my father knew him, and to my father I am indebted for what information I possess of that imposing figure—a handsome and commanding presence, enhanced in his natural dignity by the small closely trimmed beard common in those days. He appears to have been a man of varied interests, and whilst he was superintendent at Ararat he established a vineyard and cellar. Some excellent wines were produced there, and one especially, known as Golden Chasselas, achieved a deserved popularity amongst his friends.

Beattie-Smith's lectures at Kew were well given, but at that time students took no profound interest in psychiatry. Most attended either because the lectures were compulsory or perhaps in a spirit of curiosity, to see what an insane patient really looked like. The attitude of the general public, too, at that time (except of course of those who had relatives or friends in mental hospitals), was one of absolute apathy or morbid curiosity. No doubt this attitude of mind was evident enough to Beattie-Smith himself, and no doubt, too, it was for that very reason that he endowed these lectures, so that this almost universal apathy and ignorance of mental disorders might in some degree be dissipated.

If he were living now he would be most gratified at the achievement of his aim, to which this lectureship has contributed in no small measure. Public apathy has been supplanted by a general interest in things psychiatric, and by a determination to have the best possible mental health service that the community can provide. Remember this—a community will get only the health service it deserves. "Ask and ye shall receive" is as true in the temporal as it is in the spiritual life. Perhaps when it comes to matters temporal "demand" is a better verb than "ask". A determined and enlightened public demand is the best guarantee of obtaining an efficient service of any kind, whether it be transport, education, bread delivery or health.

Psychiatry itself has advanced from the purely custodial and descriptive stage which it had reached fifty years ago to a specialty which employs a wide variety of effective techniques, and which impinges on almost every aspect of general medicine.

Apart from the increasing number of young medical graduates who are embracing psychiatry itself, psychiatric thought is permeating the whole study of medicine, with incalculable benefit to both.

Pure psychiatry is no longer pure, for it has taken unto itself a mistress, at first with great misgivings, perhaps motivated by unconscious feelings of inferiority. But the

[1] Delivered at Melbourne on May 7 and 14, 1951.

liaison has been fruitful, and psychology and psychiatry are now practically man and wife.

I am very conscious of the honour accorded me in being invited to deliver these lectures this year. The fact that I must follow so many distinguished predecessors weighs heavily upon my morale. What comforts me is the knowledge that the subject is so rapidly widening that no one can be fully acquainted with all its ramifications. It seemed to me then that I would best fulfil the wishes of the founder himself by discussing with you those aspects of psychiatry in which I have had most experience, or which I deem the most important. To an audience such as this, ranging from the specialist in psychiatry to the interested layman, I apologize in advance if at times the subject matter seems too technical for the one or too elementary for the other. As far as possible those aspects of more general interest have been included in the first lecture and the more specialized material left for the second.

Before I continue with the subject matter proper of this lecture, there are several matters of a more general nature that I wish to mention.

Visitors to mental hospitals ask questions. Let me endeavour to answer a few of them. One of the commonest is: "Why is so-and-so in hospital? He is quite sane." To answer this question it might be well to give you an idea of the various types of patients likely to be found in mental hospitals, and what their requirements are.

1. First, there are increasing numbers of the senile mentally enfeebled. These I will speak of later. They require two things chiefly—the amenities of a thoughtful home and some degree of nursing, sometimes little, sometimes much and onerous.

2. Secondly, there are those sometimes called "asylum-sane". There are a number of patients who have recovered more or less completely from their acute breakdown and adjusted themselves happily to the sheltered environment of the hospital. But as soon as they attempt to take their place in the community they relapse. After perhaps several such attempts both they and the medical staff realize that they can maintain a level of adjustment only in a sheltered environment, in the small community life of the hospital. The hospital is to them an "asylum" in the old and real meaning of the word—a place of peace and refuge from the cares of the world. Talking to such a patient, you would be unlikely to detect much amiss and might wonder why he was there. Again, other patients can converse rationally and you wonder at the pig-headedness of the doctors in detaining them. Perhaps you think that the doctors just do not care, and have not bothered to talk to him for months anyway, otherwise they would be bound to see that he was sane. But do not expect every patient to be turning handsprings or shouting nonsense or listening to voices or seeing visions. There are some whose main defect is one of memory. They cannot remember what happens from day to day. Their minds are lucid enough as far as the present is concerned, but they are so crippled by this memory defect that they are quite incapable of maintaining themselves in the community. The most pronounced cases occur amongst chronic heavy alcoholics. Other patients are utterly lacking in judgement, foresight and purposive drive, but again converse apparently rationally and yet are like the last-mentioned—unable to maintain themselves because of their utter lack of common sense or plain "nous". Others again are highly delusional but extremely shrewd individuals—paranoiacs whom you might talk to for hours before you found that they really were far from being sane people. It is not uncommon for psychiatrists themselves to differ in their opinions about such a person. In such cases you will find that the one that has known the patient longest will be right.

These remarks partly answer another question: "Is it possible for sane people to be detained in mental hospitals against their will?" The answer is an emphatic "no". In spite of jokes to the contrary, most psychiatrists are fairly level-headed individuals, and why any psychiatrist should wish to keep any person unnecessarily detained in his already overcrowded hospital is quite beyond me. He achieves no benefit either to his reputation or to his pocket. His reputation depends not on how many patients there are in his hospital, but on how many he has returned to mental health. Why should a doctor deliberately expose himself gratuitously to an action for illegal detention? Even supposing the incredible happened, which would mean several doctors at least in the plot, the patient concerned has many avenues of appeal open to him—he may write to the Governor of the State, any Minister of the Crown, any Judge of the Supreme Court, the Director of Mental Hygiene, the Public Trustee. You might say his letters may be intercepted; again there are heavy penalties—such letters must be forwarded. Another safeguard is the official visitor, who may interview any patient. Consider even the extreme case of an alcoholic who is dangerously violent when drunk, who is an incorrigible drunkard and who you are morally certain will be a menace to his family or to the community within a few days of leaving hospital. A Chief Justice of Victoria has ruled most emphatically that if he is sane at the time of examination and demands to leave he must be permitted. The responsibility for his further actions, if illegal, devolves on the police not on the psychiatrist.

To return now to the types of patients in mental hospitals.

3. Thirdly, there are the schizophrenics—the majority by far and the chief subject of these lectures.

4. Fourthly, there are those with mental disorder due to brain damage—organic dementia. They will never be curable, and their requirements can be briefly stated as "a home *plus* nursing attention".

5. Fifth, there are patients with severe grades of mental defect—these are ineducable and require simply a home and care. Idiots require the same quality of care as is given to infants; low-grade imbeciles require the same quality of care as is given to toddlers.

6. The sixth group comprises patients with milder grades of mental defect. These require a home *plus* skilled training up to the maximum they are capable of absorbing. There is a certain amount of loose talk about training high-grade defectives to take their place in the community. This is false optimism. They will always need a sheltered environment with some measure of supervision—true, it may be minimal and unobtrusive with the highest, but it will be necessary. Certainly they are capable of living happy, useful lives, but only with the measure of training and supervision that I have indicated. If they do not receive this from the community then they drift into destitution and delinquency. In this connexion let me quote Penrose (1949), an authority on mental defect:

> There is an inverse relationship between the number of beds provided for the mentally ill or defective, and the number of people in prison. The provision of two mental hospital beds will make one prison cell unnecessary. Per inmate, prisons are about twice as expensive to run as mental hospitals, so that even on financial grounds, there is no loss in treating delinquency as a medical rather than an ethical problem.

7. The seventh is in many respects the most important group—it comprises those recently admitted to hospital and those recovering. They need by far the largest measure of psychiatric attention and skill, with the cooperation of many members of a team—nursing staff, psychologist, social worker, pathologist, biochemist, occupational therapist, and educational and rehabilitation officers or agencies.

These, then, comprise the bulk of the patients to be found in our mental hospitals. How are they admitted? In a number of ways. The first is at their own request, by far the most preferable, as voluntary boarders. These are people who realize that they are ill; but many mentally ill people have no realization of their illness. They are quite lacking in insight into the fact of their disorder, so evident to everyone else. Naturally they often refuse treatment, seeing no reason for it. They must be brought under treatment, against their will if necessary. They have to be deprived of (i) freedom of movement, (ii) freedom to manage their own affairs, (iii) freedom of decision regard-

ing treatment. Now this is the gravest step that can be taken against any person, and there must therefore be adequate legal safeguards to protect both the person himself and the community. The legal provisions of certification give them, and it surprises me to hear psychiatrists and others inveighing against the stigma of certification—it is not the stigma of certification, but the stigma of insanity, and of this I should like to speak later.

I have said that psychiatry has advanced in many ways since Beattie-Smith worked and taught, but it has also retrogressed in other directions. The decadent Vienna of the last years of the Austro-Hungarian Empire warped more minds than Schickelgrüber's. I believe that Freudian psychology has cast a blight upon the minds of men that will last perhaps another fifty years. I can see the hackles of most of my colleagues visibly rising at this blasphemy, for Freud is a very great god indeed. The really great error that appals me is Freud's implicit assumption of psychic determinism, the criminal's best friend for a generation. The argument has been, roughly: "Poor fellow, he couldn't help himself; he was an automaton in the grip of that ravening demon, his unconscious." Fortunately for society our clearer-headed brethren of the bar have been extremely difficult to convince of the validity of this assertion. In fact this denial of free will and hence of criminal responsibility has discredited us perhaps more than any other assertions we may make, as expert witnesses, in the eyes of the legal profession.

Lord Chief Justice Goddart was reported recently as having uttered some very pertinent remarks upon this subject:

> Beware of psychiatrists. Most approved schools will say you can usually recognize boys who've been sent to a psychiatrist. They are cocky and self-assured because they think they are interesting cases. If boys steal cigarettes, I think it is because they want to smoke, but to a psychiatrist, cigarettes become symbols of love and evil.

Lord Chief Justice Goddart does not like the term "juvenile delinquent" either—he thinks these people should be called simply "naughty boys and girls" and that they do not need a psychiatrist but "a jolly good hiding". I have a suspicion that he may not be far wrong there. And if you ask me what I would do about the young delinquent I should say that it depends upon whether he is over-privileged—spoilt if you like—or under-privileged; but it must be borne in mind that these categories have no necessary relation to economic status—many children of quite poor parents get everything they ask for.

Freud's theories of pan-sexualism and psycho-sexual development are to many, including myself, simply not true. The Freudian reply is, of course, that this is because such ideas are repugnant to me and I am therefore psycho-resistive to their acceptance. Well, I am certainly resistive to accepting anything for which I cannot see sufficient evidence; but I cannot admit to any feelings of special repugnance concerning these theories. The same applies to Freud's extravagant notions of symbolism in dreams. I find them interesting, amusing and ingenious, and in some instances undoubtedly correct, but to swallow the whole vast range of metamorphosis is beyond my digestive capacity. It seems to me at least as likely that, when a person dreams of a Zeppelin or a leaking tap, a railway tunnel or an imposing building, these things are part of the dream in their own right and not as substitutes or symbols for something else. It is at least possible that the symbolism attributed to them has been attached later during the course of the free association of an analysis. Once one is aware of what is expected in the way of symbolic interpretation, practically any form or function can be moulded in the desired direction with little or no conscious effort.

To conclude this tirade, let me utter a word of plaintive protest concerning the esoteric jargon which has grown up as part of this fascinating phantasmagoria. I think it was in a *Readers Digest* that I saw psychoanalysis defined as the art of describing the commonplace in terms of the incomprehensible.

My choice of subject inevitably falls upon that illness which is responsible for filling more than half the mental hospital beds in the world and more than a quarter of all hospital beds. In this State alone there are above 3500 schizophrenic patients living out their lives in a disordered twilight of phantasy and ureality. It is a dream world, sometimes pleasant, often a nightmare, too often a void empty of emotion and of thought. Its victims are picked with the dreadful impartiality of decimation. Intellect is no bar—it has claimed many of our brightest youth. Indeed, often enough the greater the initial endowment, the worse the disease.

It is the one major problem to be solved. The cause is unknown, treatment is only partially satisfactory.

When a problem is urgent and bewildering it is inevitable that many people have much to say. So it is here. The literature on schizophrenia is immense, much of it a tropical jungle of verbiage. Guiding principles are necessary if one is not to be hopelessly lost. For this reason I propose to devote this first lecture to a consideration of the aims, methods and results of psychiatric research. For in the pursuit of any problem it is always illuminating to see where others have succeeded or gone astray. With this background we may pursue with perhaps more profit the specific case of schizophrenia.

My qualifications for discussing medical research in general or even psychiatric research in particular are best left unstated. I might most kindly describe myself as an enthusiastic amateur, full of curiosity, with fair determination, golden opportunities, inadequate knowledge and woeful technique. But even the small boy, fishing after school in a muddy pond with string and bent pin, occasionally hauls forth a handsome fish.

There is nothing peculiar about psychiatric research except perhaps the material upon which it works. There are two chief schools or lines of research in this field. One school holds that abnormal mental states are explicable in terms of a pure psychopathology, whereas the other believes it more likely that the major psychoses, such as schizophrenia or manic-depressive insanity, are due to subtle organic or biochemical changes. Later we shall discuss this more fully.

Let us consider the main factors concerned in any kind of research. They are five: the man, the machine, the method, the material and the aim.

1. Firstly, let us consider the man. MacDougal taught that curiosity was one of the primary instincts. Be that as it may, it varies enormously in development in different persons, both in intensity and in direction, and in the same person under different circumstances and at different ages. It may take a social or an intellectual direction. In the first case we may be fortunate enough to have the first-class journalist or the bad luck to be plagued with a plain busybody. There seems to be no necessary correlation between curiosity and intelligence, although high intellect is often associated with keen curiosity. But most of us, including many highly intelligent and useful citizens, have an inescapable tendency to accept things as they are. We are content with present knowledge, we often absorb it in vast quantities and make skilful use of it, but yet have no inclination to take the initiative in extending its bounds.

Of those who do add to the total of human knowledge, some are preeminent as observers and collectors of new facts—the great naturalists and explorers—others excel at the correlation of data, some few are equally skilled at both—for example, Darwin and Pasteur.

In investigating a particular relationship of cause and effect there is a common source of error which has led many a worker along the wrong road to false conclusions, and that is the difficulty in distinguishing between temporal or spatial contiguity and real causes. If a man is killed in the jungle by a tiger it is hardly correct to attribute his death to the jungle, or to come nearer home, many people are accidentally killed on roads but not by roads. Or to give another example: there appears to be a steady increase in the incidence of carcinoma of the lung.

It is possible that I could show a close relationship between this increase and the increase in air travel or the domestic use of washing machines. But it is extremely unlikely that the relationship is any more than a temporal one.

Similarly, because schizophrenia tends to develop most often in persons exhibiting certain traits of personality, one must be careful not to jump to the conclusion, as has been done, that such traits are the cause of schizophrenia. They may merely provide for the cause the conditions under which it can operate, in the same way that exposure to cold can facilitate the invasion of the respiratory tract by, say, pneumococci.

One of the major criticisms that may be levelled at much of the work published in psychiatry is the tendency to uncontrolled observation. From my own reading the impression left by much of the literature is one of ingenious and airy hypotheses, superficially plausible at times, but too often couched in an incomprehensible jargon, and quite lacking in a foundation of solid fact. It is seldom indeed that one comes across work to compare with the recently published carefully controlled observation on the ætiology of rheumatoid arthritis by Davidson and others. That work mercilessly squashed a number of favourite notions. I shudder to think what would happen to many of our ideas of causality if they were subjected to the same rigorous test.

2. Secondly, mankind in its manifold activities has devised a multitude of machines, instruments or weapons. Each one of these must be appropriate to the task. A boy cannot knock out a tank with a shanghai, but he may well bring home a chicken. In the history of science it is evident that many discoveries could not have been made earlier than they were simply because the special instrument of discovery was not available. Histology or bacteriology could not have antedated the microscope. Lister may well have suffered the same practical oblivion as Semmelweis had he lived before Pasteur. At the present time the use of tagged atoms, or radioactive isotopes, is revolutionizing biochemistry. The difficulty about all this, of course, is that when faced with the solution of a particular problem we usually do not know whether or not we are using the correct material means. All we know is that if we do fail, that is one of a number of possible explanations.

3. Thirdly, the method or tactics or technique to be adopted in approaching a problem depend so largely on the situation that I doubt if any useful rules can be laid down; the result depends so much on ingenuity and perseverance. But one can say that an essential for successful research is thorough training in the established techniques and a systematic gathering of all known facts relevant to the investigation. Even more important, perhaps, is the determination to use any and every means to the end, no matter how humble, how unorthodox or how tedious. William Withering did not disdain to learn the use of foxglove from an old woman of Shropshire; Jenner learnt from a dairymaid that cow-pox prevented small-pox; as for tedium, how many of us would have gone as far as "606" or "914" or "693" in investigating one possibility after another?

When a new and fascinating instrument or technique has been elaborated there is often a tendency to glorify these at the expense of aim. A good present-day example is the position of that new specialty with the outrageous name of "psycho-surgery". Not for one moment do I deny the almost miraculous results of prefrontal leucotomy in carefully selected patients; but when I hear of "topectomies" and "thalamectomies" with micro-gauges and three-dimensional X-ray control, I believe that technique is outpacing knowledge. To choose another example—convulsive therapy: there is no doubt of the beneficial effect in suitable patients. But it does not matter how the convulsion in induced, whether by the older chemical method or the newer electrical, the result is the same. That is, the technique matters little so long as the aim is achieved.

4. Fourthly, we must consider the material or circumstances to be investigated. Discoveries are usually made by those who are in intimate contact with particular problems, when the problem forms part of their daily working lives. As Lancelot Hogben puts it, this is the "social context" of discovery. It is unlikely (but not, of course, impossible) that a chef would contribute much to the study of psychiatry. The ordinary untrained man in contact with a problem is much more likely to have a shrewd idea of the direction in which to seek its solution than the scientist without first-hand knowledge. For example, it was cattlemen whose herds were dying of Texas fever who put Theobald Smith on the right track. They knew that it was spread by ticks—they knew that "no ticks, no fever".

I may say here that if any young graduate wishes to carry out clinical research in psychiatry, there are unrivalled opportunities in the mental hospitals of this State, simply because of the wealth of clinical material. And speaking of opportunity, let us remember always the unexpected help that sometimes comes through advances in apparently unrelated fields of knowledge. Lister saw the connexion between wound sepsis and Pasteur's work on fermentation. It must have seemed to others at that time a long distance from ropy wine to putrid wounds.

5. Finally, let us consider the aim. We must know what we hope to discover and formulate it as explicitly as possible. Too often, as I said earlier, no problem is seen; the *status quo* is sufficient. We know just so much about schizophrenia, and that is that. The problem has been investigated exhaustively from every possible angle, and nobody seems to have advanced much further, so what can we do about it? It is rather like a people living in a remote valley surrounded by high mountain walls. Most simply accept them as unscalable, some few have attempted and failed, perhaps confirming the pessimism of the majority. But one fine day some determined group or individual finds a way and a new world is opened.

If we turn now from the general to the particular, how can clinical research best be organized in the mental health services of this State? The first thing we must decide is this: does it need organizing at all? How have the biggest advances in medical knowledge been made in the past? We must agree that many of the most spectacular have been made by individuals working largely by themselves, with a minimum of help from others and a paucity of equipment. In other words, organization is useless without ideas. But nowadays technological advances have been so great that for much work highly organized departments with equipment of almost incalculable value are essential. They must be on a national scale of endeavour.

What, then, should be the clinical research "set up"? Should it be solely individual effort or should it be on a community scale of team endeavour? The answer is that both are necessary. Sometimes a particular problem is tackled and solved by one person working alone; but other problems by their very nature require the organized efforts of a team. The temperament of the worker must also be taken into account. Some workers are naturally "lone wolves" and give of their best when left to themselves, whereas others work better under the stimulus of group activity, of competition and of the free interchange of ideas.

The organization of a psychiatric clinical research unit then should make the fullest provision for (*a*) a wealth of clinical material, and (*b*) all possible methods of investigation. No one can say of an unsolved problem that the solution lies here or lies there; so every worker must be free to choose whatever method he thinks suitable or likely to succeed in solving the riddle. As there are two main schools of thought in psychiatry—the one organicist, the other psychological—provision must be made for both. So on the one side would be needed biochemical, pathological and neuro-physiological laboratories *plus* neuro-surgical and X-ray departments, and on the other facilities for psychoanalysts, psychologists and social workers with space available for such psychological techniques as group therapy and psycho-drama.

An army is blind and deaf without its intelligence service and a clinical research unit without its library. Although

there is a library at the Receiving House at Royal Park and books are generously lent to any medical officers of the department who ask, yet the department as a whole needs a fully developed medical and psychiatric library with abstracting service and routine circulation of relevant abstracts and technical information to all members of the staff. This might well be a function of the new clinical research officer, the library to be located at the research unit.

The site of a research unit should, of course, be where there is the greatest and most varied flow of clinical material, and that is necessarily at the largest Receiving House in Victoria—at Royal Park. I understand that plans have been completed for a unit of this type at Royal Park.

What should be the aim of such a unit? Advances in psychiatry have been of two kinds: first, real advances in knowledge of causes, and secondly, empirical advances in treatment. Sometimes one, sometimes the other, has been first in a particular disorder. The cause of general paralysis of the insane was found to be the *Treponema pallidum* before an effective treatment was found in artificial fever therapy. Conversely an effective treatment for some patients at least with schizophrenia and most patients with melancholia has been discovered in insulin therapy and convulsive therapy before we have any clue to their real causes. Therefore our unit must be capable of initiating and testing new treatment, whether psychological or physical, as well as of investigating causes. This duality is important, because advances in the one field often suggest lines of investigation in the other.

Should it be a teaching unit? I believe only secondarily and in a strictly limited degree—limited, that is, to clinical meetings or lectures at no set intervals for the purpose of promulgating work done at the unit. Certainly it should not be used for routine undergraduate or post-graduate teaching, although of course graduates would be attached for training. There is no doubt in my mind that such a unit would be, more than anything else, a stimulus to the highest endeavour and professional standards in psychiatry. It would be to psychiatry what the Walter and Eliza Hall Institute and the Baker Institute are to general medicine.

How can young graduates be persuaded to devote themselves to the full-time study of psychiatry? Surely only by teachers of medicine repeatedly emphasizing the magnitude and urgency of the unsolved problems in this field. From the economic point of view alone the burden of mental ill-health is enormous.

Before I consider some of the specific problems which require solution, let me say a few words about the so-called stigma of insanity. This shame, this desire to conceal, is a very real thing. It is due primarily to fear, fear of insanity, a fear that possesses many people at one stage or another of their lives. Many people with quite minor mental maladies, a mild anxiety state for example, feel that their symptoms are those of impending insanity. This thought naturally adds fuel to their anxiety, their symptoms are aggravated, and thus it seems as if their worst fears are confirmed. This widespread fear is often enough projected as hatred or aversion of the thing feared—of insanity and all that goes with it. Why should mental disorder be so feared? The answer, I think, is relatively simple. It is because of the imputation of incurability which adheres to insanity. Incurability is due to ignorance of causes. The stigma will not be removed by palatial buildings, elaborate staff or careful euphemisms. It will disappear only when schizophrenia becomes as curable as scurvy. This brings us back once more to the fundamental need—psychiatric research.

As I have reiterated, the most important disorder to be investigated is schizophrenia, from the numerical point of view alone. In the next lecture I hope to outline for you the present state of our knowledge upon this subject. There are many other problems in psychiatry which await the investigator. Let me mention some of them.

1. There is the unsatisfactory state of understanding of many non-specific types of dementia occurring in middle life—the so-called presenile dementias. To label them as examples of Alzheimer's or Pick's disease is to do no more than consign them to a particular pigeon-hole. It is likely that some at least of the patients apparently suffering from alcoholic dementia are in this group. Recently I was able to diagnose the cause of death of a woman I had never seen, who had died at Mont Park ten years previously and in whose case the correct diagnosis had never been suspected. There was nothing particularly difficult about this retrospective diagnosis after her brother had been admitted to hospital under my care suffering from indubitable Huntington's chorea. Her history was briefly as follows: She was admitted to hospital at the age of thirty-eight years because of increasingly erratic behaviour. She was delusional and hallucinated and thought to be suffering from schizophrenia. She lived for three years after her admission, and it was noted that her speech steadily became less and less intelligible. She was also reported to be spastic in the later stages. At autopsy generalized wasting of the grey matter of the cerebral cortex and basal ganglia was found, with dilatation of the ventricles of the brain. At no stage did she exhibit the jerking incoordinate movements of Huntington's chorea, which would have made the diagnosis obvious. It is of interest that her brother's most obvious disability is in his speech. The point is this: how many aberrant cases of Huntington's chorea remain undiagnosed? It is of great importance, not to the patient, because no treatment is of any avail, but to the relatives. No brother or sister, son or daughter of a person suffering from Huntington's chorea should ever marry. The disease often does not declare itself until early middle life, by the time most people have married and borne children, and just at the time when they should be of most value to their growing families. It is the prime example of a mental disorder in which the causes are hereditarily determined—in fact, one of the very few proven examples.

Brothers (1949) has made a valuable and exhaustive research into the transmission of the disease in Tasmania, where it is by no means uncommon. He has traced 86 known cases to a common ancestor, who migrated to that State in 1848. Here is the family history of a patient who was under my care: A young man was the youngest of 11 children, of whom one had died in infancy. Of the ten who reached adult life, five sisters had died of Huntington's chorea and a sixth was known to be affected. With the patient himself this was seven out of ten, with the possibility that one or more of the remainder might later in life develop the disorder. The mother was one of three brothers and two sisters, all of whom died of the disease, and the mother's father had died of a similar disorder. Shortly afterwards another young man came under my care, also suffering from Huntington's chorea, but this time there was no family history of it—at first. However, when the question was carefully investigated it was found that he was an adopted child and the illegitimate son of the first patient's eldest sister.

This emphasizes the desirability of initiating research in human genetics in Victoria. Admittedly it is a difficult task in a young country; but if, in the Department of Mental Hygiene alone, there was some central organization for the correlation of the data of family histories, elicited perhaps from different patients in different hospitals at different times, I am sure much valuable information would emerge.

Since the work of Gregg on the relationship between maternal rubella and congenital defects, a great stimulus has been given to what had seemed previously a rather hopeless field of investigation—the causes of various forms of congenital mental defect. Of these, mongolism is one of the commonest. Up to half the babies under one year old diagnosed as suffering from mental defect are mongols. There are three reasons for this: (i) the physical features make the condition evident to the most casual inspection; (ii) in general, being frail babies, many of them die at an early age; (iii) it may be difficult to diagnose other forms

of mental defect until the children are older, especially if the defect is comparatively mild.

The extraordinary feature of the disorder is that the children all bear such a striking resemblance to each other, with their short stature, small round heads, slanting eyes, little noses with broad flat bridges, intermittently protruding tongues and short stubby fingers. A photograph of a group of mongol children suggests forcibly that they are of the same parents.

The cause is quite unknown. One fact that has been recognized for a long time is that the proportion of mongols born rises steadily with maternal age. But young mothers can bear a mongol child and then have other perfectly normal children, so it is difficult to see what effect maternal age, as such, has on causation. All sorts of theories have been advanced. An early one was that the condition was an atavism or reversion to some primitive ancestry. Germ plasma mutation, defective nidation of the ovum in the uterine mucosa, intrauterine damage by some toxic or infective factor, hormonal abnormality and nutritional defect, have all been suggested; but all unfortunately are pure speculation and in general reflect the prevailing trends in the medical thought of the day. For example, it was inevitable that mental defect should be investigated from the point of view of Rh incompatibility. Could it be responsible for any appreciable number of cases? Gilmour (1950) went into the question thoroughly and concluded that apart from the occasions when it causes erythroblastosis and kernicterus the Rh factor plays no part in the causation of mental deficiency.

Here, then, in mongolism is another problem of first-class importance crying out to be solved.

Turning to the other end of life we find that psychiatry has an especial interest in geriatrics, as age changes do not spare the brain. Mental deterioration in the aged, and the necessity for the community to make increased provision for those in the twilight of life, are becoming increasingly urgent matters. Always a proportion of such aged infirm—poor, frail, confused, restless old people—have been admitted to mental hospitals, simply because they have no relatives to care for them or because their nursing imposes too large a burden upon the family. The numbers are steadily increasing with the increasing proportion of old people in the community. It is wrong that they should have to be sent to mental hospitals, nor are such hospitals generally designed for such patients, although of course there are infirmary wards. But these are becoming increasingly overcrowded, and the overflow of old patients must be distributed in other wards, to the detriment of the old people themselves and of the normal function of the ward. Psychiatry must share the burden of care, investigation and treatment of such patients. But it would be kinder of the community to insist on special hospitals for the aged infirm. Their special problems could be investigated and treated far better, and such a move would enhance considerably the efficiency of mental hospitals, overcrowded as they now are.

Does this or that discovery mean that more patients can be assisted to improvement or recovery? This, after all, is the only real criterion of successful psychiatry. The Victorian Department of Mental Hygiene has come in for a lot of criticism in recent years, so let us examine its record from the one point of view that matters—therapeutic success or failure. The facts are incorporated in that very dry publication, the annual "Report of the Director of Mental Hygiene". When analysed year after year they tell a story of steady progress in successful treatment of some disorders, but they also show that enormous strides have yet to be made in treatment of others. Let us take some of the more important disorders. First of all, that once dread disease, general paralysis of the insane—it has almost disappeared. If our hospital admission rate was on the same scale as in 1913, when "Salvarsan" was first introduced into general use in this State for the treatment of syphilis, there would now be approximately 125 admissions per year to Victorian mental hospitals. But the incidence of general paralysis has steadily diminished since that year, apart from a slight rise in the middle 1930's probably due to infections contracted and inadequately treated during the first world war. In 1949 there were only 15 admissions (certified patients). The obvious comment is that this reflects credit, not upon the psychiatrists, but upon the venereologists. This is true; but if you examine the figures further you will find that the picture alters radically after 1926, when malarial treatment was introduced here by R. S. Ellery. Up to that time deaths closely paralleled admissions. Most paretics died in one to two years in a state of the profoundest dementia—mindless, paralysed and incontinent. After that time you find two new phenomena: first, an appreciable although low proportion of real recoveries, perhaps about 10%, and second, a steady rise in the number of "arrested" cases, which has now probably reached its peak of approximately 120 and will slowly diminish if the present admission trend continues. Those patients with the arrested disease would have died years ago if they had not had malarial therapy. Why should there be such a high proportion of arrested cases suffering from a varying but crippling degree of mental enfeeblement? The answer is simple. As F. M. G. Prendergast and others have pointed out, their condition has not been diagnosed early enough. That is not usually the psychiatrist's fault. The treponema has wrought irreparable damage in the central nervous system. Malaria can be regarded as truly curative in the sense that it successfully destroys the causative agent; but it is beyond human skill or the habits of Nature to replace nerve cells already destroyed. Since the end of the second world war penicillin has been increasingly used in the treatment of general paralysis, either alone or combined with malaria. As far as can be seen at present the results are substantially the same with malaria alone, penicillin alone, or both combined. Good results are far more dependent upon early treatment.

The general paretic frequently has no realization of personal illness or suffering; but the melancholic is sunk in the utter depths of loneliness, despair and self-reproach. It is probably the most fearful disease that man can suffer. No physical pain can compare with this agony of mind. It is little wonder that such patients seek the escape of self-destruction.

Until 1937 nothing could be done for these depressed ones, apart from attempting to take the edge off their misery with various sedative régimes and waiting for the gloom to lift. In that year "Cardiazol" convulsive treatment, initiated by Meduna of Budapest, was introduced to Victoria. The story of convulsive therapy illustrates well the theme that often in science one aims at one object and hits another. No doubt the moral is to go out shooting anyhow—you are bound to bring something home.

Meduna thought there was some biological antagonism between schizophrenia and epilepsy, because they appeared to him mutually incompatible. He speculated that if he gave his schizophrenic patients convulsive seizures he might cure them. The new convulsant drug, "Cardiazol", was "tailored to order", and when used certainly did produce improvement in quite a number of schizophrenics. But it was soon found to be far more effective in banishing depression. As a result it rapidly became the standard treatment for melancholia. Results were often dramatic. The condition of some patients who had been profoundly depressed for months or years cleared up completely in perhaps two weeks. During and since the war therapeutic convulsions have been induced by electrical rather than chemical means, largely for technical reasons. The results are the same.

Unhappily there is a proportion of melancholics who do not respond to this treatment, and there are others who, although responding, soon relapse. It is for these patients that prefrontal leucotomy is indicated and has scored its most brilliant results.

Before the advent of these modern forms of treatment the admission rate of melancholic patients into the mental hospitals of Victoria was nearly 100 per year; that is, in the early and middle 1930's. The spontaneous recovery rate was about 38%. In the late 1940's the admission rate

averaged about 60 per year and the recovery rate about 50%. This admission rate is only a little more than half the number expected when calculated from the admission rate of fifteen years previously, and when allowance is made for the increased population. In other words, nearly half the melancholics are being so successfully treated that they are never admitted to mental hospitals. The figures for recovery in mental hospitals are not very impressive even with modern treatment—50% against the spontaneous rate of 38%. But remember that those admitted to mental hospitals must include most of those who have failed to respond to treatment elsewhere.

Now let us consider *dementia præcox*, our largest problem. The average yearly admission rate for the period 1931 to 1936 inclusive was 133·5, and for the period 1944 to 1949 it was 175. The average recovery rate for the period 1931 to 1936—that is, prior to the introduction of insulin and "Cardiazol" therapy—was 22%. For the period 1944 to 1949 the recovery rate averages 39%.

We can draw the following conclusions. First, there has been no diminution in the admission rate of patients suffering from *dementia præcox* as there has been for melancholia; in fact, there is an increase greater than the proportional increase in population. Therefore treatment of such patients outside mental hospital must be either on a very small scale or relatively ineffective, unless, indeed, there has been a real increase in the incidence of the disorder—a point worth investigation. Another possibility is that it is being diagnosed more frequently.

If we turn to the recovery rate in mental hospitals, although it has almost doubled it is not nearly good enough. In early cases we know that, with a full course of insulin coma treatment, sometimes reinforced with convulsive treatment, there is an immediate recovery rate of 70% to 80%, and Webb and Noall (1949), in a valuable ten-year follow-up of insulin-treated patients, have shown that the ten-year recovery rate is 37% even when a considerable proportion of the patients initially treated were not in the early stages.

Probably the main reason for the discrepancy between the actual and the potential recovery rates is that, owing to chronic staff shortages, full coma insulin treatment cannot be given to all patients who need it as it is time-consuming and adequate trained staff is essential. It is a tragic story, but one common to many hospitals these days.

You will notice that most of the advances I have mentioned have been improvements in treatment. They have not increased notably our understanding of the real causes of these diseases.

The converse is also true—that in a number of those mental disorders of which the pathological basis has been unravelled, such as various organic diseases of the brain like arteriopathic dementia, little or nothing has been discovered in the way of successful prevention or treatment. Hence the necessity, as I have mentioned earlier, of combining in any clinical research unit research into treatment as well as into causes. The two forms of research are complementary, treatment perhaps being the more important. A patient and his relatives are far more interested in cure than in causes.

Psychiatrists must be prepared to use any knowledge or technique in the whole field of medicine in approaching the problems of cause and treatment. They must therefore have a good training in general medicine. They must be, in effect, physicians specializing in psychiatry.

I might conclude this first lecture with a plea. Let each one of us engaged in the treatment of mental illness deliberately set out to investigate for ourselves some one of the numerous problems which arise, according to our own particular training or enthusiasm. Let us never rest content with the present bounds of knowledge. It is for us to initiate a particular approach to a psychiatric problem, and if we have not the necessary knowledge or technical training—if, for example, it involves a specialized knowledge of biochemistry or physiology—then let us cultivate and coopt our colleagues in those specialties.

THE LITHIUM TREATMENT OF MANIACAL PSYCHOSIS.

By C. H. NOACK,
Mont Park Mental Hospital, Melbourne,
AND
E. M. TRAUTNER,
Department of Physiology, University of Melbourne.

IN recent years lithium salts have been widely used in the United States of America as a substitute for sodium chloride, especially in cardiac disease and hypertension (review by Talbot, 1950). Cade (1949) claimed great benefit from lithium medication in states of psychotic excitement, but its use has been discredited since several fatal cases of poisoning were reported in the United States as well as in Australia (Corcoran *et alii*, 1949; Hanlon *et alii*, 1949; Roberts, 1950). We have treated over 100 patients with various mental affections with lithium for periods ranging from two weeks to over one year, with a special view to observing the incidence of toxic symptoms and their relation to the desired therapeutic effect. In cases of mania alone considerable clinical improvement occurred, and these only will be discussed in detail. In paranoidal cases no benefit resulted, the depressive phase of manic-depressic psychosis was unaffected or even aggravated, whilst excited schizophrenics were temporarily quietened but there was no effect on the underlying thought disorder. The sedative effect of lithium was in some cases superior to that of bromides, barbiturates or paraldehyde. The use of lithium as a sedative in epilepsy has long been known.

Dosage.

The dosage employed was 0·6 gramme of lithium carbonate or 1·2 grammes of lithium citrate, three times per day after meals, preferably in tablet or capsule form. Lithium chloride was found to be much less effective. In the absence of toxic symptoms this dosage was continued until the mania abated, usually after three to seven days, and maximum improvement was shown. The medication was stopped when the patient became depressed, but if this did not occur an attempt was made to establish a maintenance dose. This dose varied greatly with each patient; some required amounts equal to those given in the acute phase, whilst with others the dosage could be considerably reduced, or even stopped altogether, to be recommenced at the first signs of recurring excitement. Patients whose maintenance dose was greater than 0·3 gramme of lithium carbonate (or 0·6 gramme of lithium citrate) three times per day were often allowed one lithium-free day per week.

Lithium Poisoning.

Some patients did not appear to be affected by the dosage used, while others suffered some initial discomfort regularly when administration of the drug was recommenced. Toxic symptoms were not observed before the third or fourth day of administration. The onset was mild, but the symptoms increased in severity if full dosage was continued, though never, even on prolonged high maintenance dosage, did a sudden incidence of grave symptoms occur. The syndrome varied greatly, but any one patient tended to maintain a constant pattern each time he neared a condition of intoxication. Even if the patient himself did not complain, some of the signs at least could not escape a trained observer. There is no danger that early lithium intoxication will be overlooked.

The symptoms included the following: gastric disturbances such as anorexia, nausea, vomiting and diarrhœa; motor disturbances, such as muscular weakness and uncertain gait, muscular hyperirritability, fasciculation which was particularly noticeable in the muscles of the face, tremor, ataxia, slurred speech; blurred vision, possibly due to poor accommodation; dizziness and vertigo; and circulatory

collapse. The syndrome was the same as that described by Cleaveland (1913), by Corcoran (1950) and by Hanlon (1950). Most of the symptoms resemble those of Addison's disease or sodium depletion. The suggestion that lithium owes its effect, at least in part, to a displacement of sodium from the body fluids and tissues appears to be mainly based on this similarity, and on the observation that massive doses of 1% to 2% sodium chloride solution act as a prompt and effective antidote (Corcoran, 1950, *et alii*).

Single therapeutic doses of lithium salts produce during the following eight to twelve hours an increase in alkalinity of the urine amounting to 1·0 to 2·0 pH units, together with a higher excretion of sodium, but also of potassium and probably to a lesser degree of other cations. A detailed investigation of the changes caused in the ionic composition of blood, plasma and urine in the healthy as well as in the maniacal patient is being carried out and will be reported in a following publication. It can, however, already be stated that no clinical evidence of any serious ionic deficiency was ever observed even after months of continuous medication. It appears that the organism responds to prolonged ingestion of lithium by adaptation. Even if toxic symptoms were present during the first few days of the treatment, a fairly steady state was usually established after ten to fourteen days. This stable state, with no more discomfort than a slight tendency to sleepiness in some cases, appears to persist during the maintenance treatment; but it is likely to be upset by intercurrent diseases, grave dietary changes, and other not always determinable factors. The effect of sodium chloride medication in lithium poisoning is possibly not so much due to correction of sodium depletion as to efficient elution of the lithium stores present in the organism.

In none of the patients treated by us has any serious condition of lithium intoxication been observed, and in none was sodium medication necessary. Ashburner (1950), in over 50 cases, encountered no serious accident. This may partly be due to the fact that no lithium-containing or other salt substitute was used, and that no attempts were made to restrict the salt intake of the patient or to alter the diet. It is likely that, with the dosage of lithium used, the sodium content of the food was sufficient to prevent the development of grave toxic symptoms. In cases in which mild toxic symptoms were observed at the beginning of the treatment the dose was halved and the patient carefully observed, since many patients show some toxic symptoms before reaching adaptation. If the symptoms increased in severity lithium medication was interrupted, but after a few days started again at a lower dosage. If toxic symptoms appeared during maintenance treatment without any signs of intercurrent disease, the medication was merely interrupted for a few days. If such patients were released from hospital, they and their relatives were warned of the symptoms and instructed to stop lithium ingestion at the first signs of discomfort or intercurrent illness and to present themselves for medical examination.

Lithium Level and Clinical Conditions.

Of a single dose of a lithium salt taken by a normal person, over 50% is excreted at a brisk rate within six to seven hours; the rest is tenaciously retained and excreted at a low, very gradually decreasing rate during a period of up to ten days. If a second dose is taken soon after the first, its effect is not cumulative, since the total amount of lithium retained is only slightly increased. Continuous medication can be adjusted so that each dose is excreted at the same rate as it is ingested, while a fairly constant level of retained lithium is maintained. The therapeutic effect of the maintenance treatment is considered to be due not to the impact of each single dose, but to the constant lithium level established. Owing to the slow excretion of the retained lithium, one or two lithium-free days do not effectively lower this lithium level; but after four or five days symptoms may recur if the patient still has a tendency to mania.

The amount retained by healthy persons varies with the individual, the dosage, the diet (salt and fluid intake) and probably other factors. We found on ourselves that after three days' ingestion of a moderate dose between one-half and two-thirds of the daily intake was found in the next fortnight's urine, allowance being made for the last dose taken. Maniacal patients appear to retain considerably higher amounts at the beginning of the treatment. It is almost impossible to obtain reliable twenty-four-hour specimens from these patients, but such samples as can be obtained during the first few days may contain very little or no detectable lithium; symptoms of poisoning may appear and there is still no satisfactory excretion. Then, quite abruptly, profuse elution starts coincidently with the reduction in the maniacal symptoms.

It is considered that the degree of lithium retention and the patient's tolerance to it determine the therapeutic effect. The lithium level necessary to terminate mania is probably always reached only by near-toxic dosage, but the two effects may not be closely related. Some patients do not suffer any toxic complications, while with others these symptoms may be grave enough to necessitate interruption of the medication before any effect on the mania is noticeable. These latter patients may, however, have their mania terminated if, after a few days, the treatment is recommenced at a lower, slowly increasing dosage. The question seems to be whether and how an efficient lithium level can be established. It will further appear that the adaptation to continued lithium medication affects mainly the liability to toxic symptoms; there is no evidence that even on very prolonged medication the effect on mania decreases. Another pertinent consideration is suggested by the observation that, at least in some cases, the lithium level established by constant medication varies, possibly with the mental condition. If after months of continuous treatment the drug is withdrawn, considerably less lithium may be found in the subsequent urines than appeared to have been retained by the same patient at the onset of the treatment.

High urinary lithium concentrations do not seem to have any significance other than showing satisfactory elution. Single specimens from the same patient may vary greatly in content, according to whether they are collected a short time after the last dose or in the interval between doses; twenty-four-hour specimens from patients on maintenance dosage have a content only slightly less than the intake. But lithium is also excreted in the fæces and in sweat, and agitated maniacal patients may excrete considerable quantities in the sweat. However, prolonged low values in all specimens obtainable may indicate excessive retention and call for a careful observation of the patient.

Talbot (1950) holds that no lithium poisoning need be feared if the plasma content is less than one milliequivalent per litre, and reports that a patient with as much as 2·9 milliequivalents per litre showed no signs of intoxication. The highest plasma level observed by us in a patient was 2·1 milliequivalents per litre, with no signs of poisoning. The highest value observed on ourselves was 2·0 milliequivalents per litre after the intake of 50 milliequivalents (1·7 grammes) of lithium carbonate within two hours. Only slight gastric discomfort was felt. The average values are of the order of one milliequivalent per litre. Since the amounts of lithium retained in the organism are between 20 and 50 milliequivalents (possibly still higher at the onset of the treatment before the patients begin to excrete it copiously), it will follow that the bulk of the lithium has left the extracellular fluid and entered the cells. The plasma level observed does not therefore reliably indicate the amount of retained lithium or the degree of "saturation"; it indicates merely the lithium in circulation. The relation between intracellular lithium content, plasma level and rate of urinary excretion appears to be variable. High plasma levels may precede massive excretion, but low levels do not necessarily exclude the imminence of toxic symptoms.

The excretion of lithium reflects the clinical state, in so far as maniacal patients tend to retain lithium as long as the mania lasts and begin to excrete it as soon as the

maniacal state begins to abate—and possibly retain it again when another maniacal attack is imminent. However, when the imminence of toxic complications is being assessed, excessive retention of lithium and high plasma values are danger signals only and uncertain in their significance. So far it has not been possible to find a laboratory test which would indicate optimum dosage or impending intoxication, and which could replace the careful observation of the patient, particularly during the time when the maniacal phase abates.

Therapeutic Results.

Over 30 patients with mania have been treated with lithium during the last two years. In only one case was the medication stopped after a fortnight when no improvement was shown; this patient also failed to respond to electro-convulsive treatment. Two patients who were so debilitated as to make electro-convulsive treatment hazardous had their mania terminated and controlled by lithium. In four cases it was necessary to supplement lithium therapy with one to three electro-convulsive treatments. Twenty-four patients have been under continuous observation for periods exceeding one year; 20 of these could be stabilized on a maintenance dosage; during twelve to eighteen months of observation none of these became maniacal while following their instructions. Four patients could not be released from hospital because of lack of suitable domestic conditions. The other 16 were released. Ten are out of hospital, either receiving a maintenance dose or with instructions to recommence lithium medication at the first signs of maniacal symptoms. Six returned with maniacal symptoms; of these, three are recurrent alcoholics and cannot be trusted reliably to continue their medication; the other three had stopped lithium therapy because they "felt it was no longer necessary". These six patients returned promptly to normal when the dosage was recommenced.

In four out of these 24 cases a maintenance dosage could not be established. In one of them, a case of chronic mania, lithium produced but little effect; in two cases in which the mania was complicated by a paranoidal condition, lithium produced a good effect on the mania but none on the paranoidal state. The fourth patient was so strongly opposed to any form of medication that lithium therapy could not be continued, though she showed great improvement while taking it.

Reports of Cases.

Two case histories will be given to illustrate the course and considerations of the treatment.

CASE I.—P.C., a married woman, aged forty-six years, has had attacks of mania and of depression for over ten years and was frequently in mental hospitals. She has been under our observation for the last twenty-one months, during which time her mental condition has rarely been normal. If she is untreated, her depressed periods usually last about fourteen days, after which she becomes increasingly maniacal and may remain so for weeks or months. On lithium medication (0·6 gramme of lithium carbonate three times per day) the mania begins to abate in about four days and disappears in from five to twelve days, according to the severity of the attack. Unless lithium therapy is then stopped she becomes progressively more depressed and remains depressed as long as the medication is continued; if it is stopped she remains mildly depressed for about a fortnight, when a new attack of mania begins to develop. The cycle has been observed 15 times. With prompt start of lithium medication at the onset of the maniacal phase, and its interruption when distinct improvement was observed, it was possible to maintain the patient at her optimum condition of mild hypomania alternating with mild depression. She has never shown signs of lithium intoxication.

CASE II.—R.N., aged seventy-two years, with severe arteriosclerosis and mild senile enfeeblement, became maniacal after a prostatectomy in October, 1948. He had never shown maniacal or depressive symptoms previously. In December, 1948, he had electro-convulsive treatment with only transient improvement. In September, 1949, he was still maniacal, aggressive, abusive and sometimes violent. Lithium citrate, 1·2 grammes three times daily, was given from September 19, 1948. After six days improvement was noticeable. On October 4 he was distinctly quieter; on October 14 he was, on the evidence of friends and relatives, in his normal, prepsychotic condition. He was then released from hospital with the same lithium dose as maintenance dosage. On November 21 he began to feel weak, tremulous and confused; on November 28 he returned to hospital. Clinical examination revealed bronchopneumonia, possibly combined with mild lithium intoxication. Lithium treatment was stopped, and the pneumonia treated. On December 8 the pulmonary signs had cleared, but he began to be restless, troublesome and aggressive. Lithium citrate therapy was recommenced, a dose of 0·6 gramme three times a day being given, increasing to 1·2 grammes three times daily by December 11, when his condition was improving. On December 26 he was "quite well, just as he had been for years before the operation". On January 23, 1950, he was confused, with slurred speech, and lithium therapy was stopped for two days and then recommenced at half-dosage. On February 11 he left hospital taking a maintenance dosage of 0·3 gramme of lithium carbonate three times daily. On April 22 he was returned to hospital because of his senile confusion, but without signs of either mania or lithium intoxication. When lithium treatment is stopped he becomes maniacal and stays so until lithium therapy is recommenced; he is never depressed.

This case is quoted in detail to illustrate that the risk of lithium medication in full dosage, even with a physically and mentally enfeebled patient, is not greater than, for example, that of digitalis medication; the toxic symptoms subside rapidly when the medication is suspended.

Fatal Chronic Psychosis Treated with Lithium.

Although no dangerous complications were observed by us, by Ashburner (1950), or by others according to personal communications, it does not appear to be justified to accept the lithium treatment of mania as invariably safe. Several fatal cases have recently been reported which appear to have in common the occurrence—possibly after initial symptoms of typical lithium poisoning—of grave symptoms entirely different from those usually encountered, and not easily explained by the action of lithium alone. Roberts (1950) reported the death of a woman suffering from chronic mania, but otherwise healthy, after only eight days of lithium medication on the same dosage as advocated here. On the eighth day the patient was confused and ataxic and vomited; lithium therapy was discontinued immediately. On the next day the patient had a major epileptiform seizure; on the tenth and eleventh days she remained confused, but the ataxia diminished. On the fourteenth day she had a series of epileptiform seizures and passed into coma with severe circulatory failure. She was treated with oxygen inhalation, nikethamide, procaine penicillin and saline given rectally and nasally, and fed nasally; the condition improved only temporarily, varying between coma and semi-coma. From the seventeenth day on her temperature and her pulse and respiration rates increased. On the nineteenth day she died after the temperature had risen to 105·5° F., the pulse rate to 150 per minute and the respiration rate to 44 per minute. The urine during this time contained a little albumin but no sugar; the post-mortem examination did not reveal the cause of death. There was no cerebral œdema, hæmorrhage or thrombosis, and no evidence of pneumonia or cardiac disease. A similar case was observed by Dr. J. F. C. Cade (personal communication). This patient suffered from chronic mania and was in failing health and near exhaustion when the treatment was started. In this case desoxycorticosterone produced temporary improvement, but it was not given in frequent or massive doses. A third death, that of a patient suffering from schizophrenia, appears to have occurred in Western Australia (personal communication from Dr. Cade).

These three patients showed the unusual symptoms of convulsions followed by coma with muscular hypotonus, which have never been observed in lithium poisoning either intentionally or accidentally induced in otherwise healthy persons (Cleaveland, 1913; Talbot, 1950); nor were these symptoms observed in the fatal cases reported by Corcoran *et alii* (1949) and by Hanlon *et alii* (1949), in which patients suffering from grave cardiac or circulatory disease

were maintained on a sodium-poor diet with uncontrolled use of lithium-containing salt substitutes. On the other hand, the patients did not show the generalized tremors, the severe degree of myoclonic twitchings, hypertonus, and tetanus-like neuromuscular hyperirritability, which were so pronounced in Corcoran's and Hanlon's patients even during the final comatose state. In the absence of further and more detailed observation, no suggestion can be made as to why these three patients reacted so catastrophically to so short a period of lithium medication. It must be assumed that, apart from the usual lithium intoxication which is quickly cured by withdrawal of the drug and sodium administration, there is as a rare occurrence the possibility of a "lithium-caused collapse" which leads to convulsions and death in coma, and which is resistant to therapy. Its causes, and particularly the factors leading to epileptiform seizures and *status epilepticus*, are difficult to explain, particularly if one recalls that lithium bromide has been widely used in the treatment of epilepsy and is listed in the "British Pharmaceutical Codex" (1950) as a form of medication in this disease. Furthermore, some decades ago, all sorts of lithium salts were extensively used—and some still are—against gout and rheumatism in a dosage sometimes as high as advocated here, without—to our knowledge—any records of intoxication with epileptiform symptoms. A further point of interest is that according to all our observations even a massive dose or a high level of lithium is excreted within four to five days and reduced to a level safely below toxicity (compare also Cleaveland, 1913). None of these patients suffered from anuria, and it is difficult to understand why the effect of the drug should have persisted for eight to ten days after the medication had ceased. It would appear that in these patients the onset of grave symptoms was caused by lithium medication, but that they were not relieved by its withdrawal, and by the usual antidote, sodium chloride. It would seem that in some cases of grave psychosis essential biological systems are strained to the verge of exhaustion and no longer possess sufficient adaptability to adjust themselves to the initial stress produced by lithium on the ionic composition of plasma and tissues.

Conclusions.

Lithium treatment was found to be very beneficial in terminating and preventing the maniacal phase in cases of mania, hypomania and recurrent mania. Poor results were obtained in some cases of long-standing severe mania, and the treatment was useless in the depressive phase of manic-depressive psychosis. The treatment was easily applied and controlled. In most cases a maintenance dosage could be established and followed by the patient himself after release from hospital. No cumulative effects or incidents of grave intoxication were observed in our patients. In only one of over 30 cases of mania was lithium therapy discontinued when it produced no beneficial effect within two weeks. In all other cases distinct improvement was observed and the drug maintained its efficacy during maintenance dosage or when its administration was recommenced at the onset of fresh attacks of mania.

The critical considerations with regard to the possibility of poisoning appear to be as follows. (i) At the start of treatment in the acute maniacal phase lithium is retained. The danger of toxic symptoms is highest when there is a maximal rate of improvement in the mental condition and during the first few days after the maniacal attack has been terminated, since it is often necessary to push the dosage to near-toxic levels to produce full improvement. Once massive urinary excretion has started the patient approaches adaptation. (ii) If a large maintenance dosage is found necessary to prevent relapses (over 0·3 gramme of lithium carbonate three times daily), it is thought advisable to allow one lithium-free day each week. (iii) At the onset of any intercurrent disease, whether this disease is likely grossly to disturb the metabolic balance or not, it appears best to suspend the treatment and to recommence it at about half the dosage after a few days, or when maniacal symptoms reappear. (iv) The same consideration applies to the suitability of the case for lithium medication. A stable condition of debility, enfeeblement, hypertension, cardiac disease or arteriosclerosis is not necessarily a contra-indication, but it may be dangerous to start lithium therapy during a period of progressive deterioration of the patient's health. (v) Lithium treatment is not promising and is possibly dangerous in cases of grave chronic mania, in which the clinical history does not show even a tendency to temporary remissions or fluctuations of the condition.

Keeping these factors in mind, we did not meet with any serious cases of intoxication among over 100 patients suffering from different mental diseases. In view of the very beneficial effect of the drug in the cases of mania reported, it does not appear to be justified to abandon lithium as a form of medication solely because some fatal cases have been reported in which lithium poisoning has been incriminated; it appears rather that attempts should be made to establish clinical criteria which will result in a better selection of suitable cases.

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SOME ASPECTS OF THE NATURAL HISTORY OF HYPERTENSIVE VASCULAR DISEASE.[1]

By BASIL S. HETZEL, M.D.

From the Institute of Medical and Veterinary Science, Adelaide.

THIS study presents an analysis of some of the clinical features of a series of 203 patients suffering from hypertension and hypertensive vascular disease. An attempt has been made to define more clearly the nature of the clinical problems associated with hypertension as it is found in Australia. The development of knowledge of hypertensive vascular disease has been comprehensively reviewed by Bechgaard (1946). In this paper reference will be made to relevant contributions as the various aspects are considered.

SCOPE OF INVESTIGATION.

The cases for this investigation have been gathered over a period of approximately two years from the wards and out-patient departments of the Royal Adelaide Hospital, with the cooperation of the honorary and resident medical staff.

An organized plan of clinical and laboratory investigations was followed in each case in the series, except in a few instances in which the patients were too ill. This comprised a full medical and social history taken from the patient personally, with a complete physical examination. Special investigations have included the following: (i) repeated examination of the urine for cells, casts and

[1] Substance of a paper read at a meeting of the South Australian Branch of the British Medical Association on February 22, 1951.

organisms; full investigation of renal function by combined urea concentration and clearance tests and excretion pyelography; (ii) X-ray examination of the chest for heart size, and electrocardiography; (iii) estimation of the basal metabolic rate and other endocrine investigations as indicated. Special attention has been paid to adrenal cortical function in these cases; a preliminary communication on this aspect has appeared (Hetzel, 1950), but the question will not be discussed in this paper.

The progress of the patients has been followed as closely as possible within the last two years. It is hoped that this part of the investigation will be continued, and that a five-year follow-up of this series of patients will be carried out.

THE SERIES.

It is considered that this series provides a reasonably good sample of patients with severe hypertension coming from a public hospital population. In Adelaide, apart from a wealthy minority, the hospital treats patients from all social classes.

The essential feature of the cases was the presence of hypertension of a degree which was clinically significant because either it was associated with evidence of hypertensive vascular disease or it was severe enough to be of importance on its own account when considered in conjunction with the patient's age (for example, a diastolic pressure greater than 100 millimetres of mercury in a patient aged less than forty years).

This has meant that not every patient examined in the hospital simply with a blood pressure greater than 160 millimetres of mercury, systolic, and 100 millimetres, diastolic, has been included in the series. For example, many patients aged over fifty years, with diastolic blood pressures between 100 and 110 millimetres of mercury (inclusive), have not been included as their hypertension is probably of little clinical significance, as Master *et alii* (1943) and others have shown. Cases of systolic hypertension have also been excluded.

It is, of course, most important to have the patient at rest mentally and physically when the blood pressure is taken, otherwise hypertension will be found more often than a normal blood pressure. Even if the patient appears outwardly calm, he or she may be emotionally disturbed.

Classification.

The present generally accepted classification of chronic diastolic hypertension is in two main categories: (i) "primary" or "essential" hypertension, when the ætiology is unknown; (ii) secondary hypertension, when the ætiology is known.

In this series primary hypertension was found in 180 cases (88·7%) and secondary hypertension was found in 23 cases (11·3%). The low incidence of secondary hypertension is in accord with general experience (Page, 1945).

Age Distribution.

The age distribution of the two groups was found to be as shown in Table I.

It will be seen that 22 of 23 cases of secondary hypertension occurred in patients under the age of forty-one years (21 under forty years), whereas most of the cases of primary hypertension occurred in patients over the age of forty years. However, it will be seen that a considerable number of cases (54) of primary hypertension occurred in patients aged under forty-one years. Sixteen of these could be regarded as early cases, 38 being fairly severe. This means that primary hypertension was still somewhat more common than secondary hypertension in this age group, contrary to the experience of Platt (1948), who found 25% only of cases of primary hypertension in a series of 64 cases. In this series, 38 out of a total of 60 cases of severe hypertension in patients aged under forty years were primary—that is, 63%. Thirty-one of these 54 cases of primary hypertension in patients aged under forty years were in women and followed toxæmia of pregnancy, so that this group is responsible for the preponderance of cases of primary hypertension. It is possible that some of these may prove to be of renal origin, although there is not sufficient evidence to diagnose renal hypertension at present. They have been regarded as "primary" in accordance with the view of Browne and Dodds (1939), who maintain that most women who develop toxæmia would have developed hypertension in any case.

TABLE I.

Age Incidence of Primary and Secondary Hypertension.

Type of Hypertension.	Age in Years.					Total.
	15 to 30.	31 to 40.	41 to 50.	51 to 60.	61 to 70.	
Primary ..	13	41	72	38	16	180
Secondary ..	12	10	—	1	—	23
Total ..	25	51	72	39	16	203

No less than 70% of the patients with primary hypertension are aged fifty years or under. This was particularly so in the case of the women, of whom 88 out of a total of 106 (83%) fall into this age group. In the men 38 out of 74 (or a little more than 50%) occur in the same group.

The proportion of male to female was 74 to 106. This was probably not a true index because of the well-known social factors which cause women to seek medical advice much earlier than men, who tend to keep on working as long as possible for economic reasons. It will be seen below that the disease in the women was not so severe as in the men. The possibility of sympathectomy led to the admission to hospital of more women, especially those aged less than fifty years. This applied to a much more limited extent to the men, and is probably the reason why there was not a higher proportion of men aged under fifty years.

It is considered that these figures, taken in conjunction with the history of duration of the hypertension, indicate that significant hypertensive vascular disease is usually manifest in some way by the age of fifty years.

Ætiological Factors.

Secondary Hypertension.

The commonest cause of secondary hypertension was renal disease—chronic glomerulonephritis (occurring in 17 cases) and chronic pyelonephritis (4 cases). In the other cases hypertension was due to presumed lead nephritis (one case) and pituitary basophilia producing Cushing's syndrome (one case). Adrenal cortical tumour and the chromaffin tumour (phæochromocytoma) were looked for many times, but were not found in any case. Coarctation of the aorta was also not encountered. One patient who had polycystic kidneys with normal blood pressure but a history of hypertension was examined, but was not included in the series. No case of unilateral renal disease causing hypertension was diagnosed in this series.

The criteria for the diagnosis of renal hypertension were as follows.

1. In the case of chronic glomerulonephritis one or more of the following associated features had to be found to justify such a diagnosis: (*a*) a history or evidence of subacute nephritis, the Ellis (1942) classification being used—either acute nephritis (Type I) which had not cleared up, or a Type II nephritis with œdema and albuminuria; (*b*) presence of impaired renal function in a patient aged under forty years; (*c*) a history or the presence of albuminuria in a patient aged under forty years. It is not uncommon to find (*b*) or (*c*) without evidence of (*a*). It is considered that this is due to glomerulonephritis which has never manifested itself as recognizable Type I or Type II nephritis. Either albuminuria or evidence of

impaired renal function alone in patients aged over forty years has usually been considered the result of hypertension, and not as an indication of preexisting renal disease; this is in agreement with Platt (1950).

2. In the case of chronic pyelonephritis evidence of a gross renal lesion in association with hypertension in a subject aged under forty years (especially a male subject) appears almost certainly to be of ætiological significance. But with regard to patients aged over forty years (especially women) the position is different. Chronic urinary infections have been found so commonly in women during this investigation (20%) that coincidence with hypertension must be very common. For this reason, when chronic pyelonephritis has been found in women aged over forty years, it has not been considered the cause of their hypertension unless there was other supporting evidence. Nearly all the patients in the original cases of Longcope (1937) were aged under forty years.

Primary Hypertension.

Under the heading of primary hypertension are grouped all cases in which definite clinical evidence of the known causes of secondary hypertension is lacking. The absence of such ætiological factors is the only common feature of this group. The homogeneity or otherwise of these cases of primary hypertension was given special examination in this study.

An investigation was made into the incidence of various factors in primary hypertension which had been held by various authors to be associations that might be of ætiological significance.

Table II shows the incidence of five of these factors: a family history of hypertensive vascular disease, the presence of undue stress in the environment, obsessional compulsive personality traits, obesity, and any suggestive evidence of endocrine disturbance.

For the family history to be regarded as significant, at least one close relative (father, mother, brother or sister) or more than one distant relative should have had some manifestation of vascular disease—for example, sudden death, stroke, Bright's disease, dropsy or high blood pressure—by the age of sixty years.

It will be seen that in 33% of the cases this history was found much more commonly in women (43%) than in men (19%). In approximately half of these cases with "positive" family history such manifestations occurred in more than one close relative.

Platt (1947) found the family history "positive" in 76% of cases, but his report shows that he was not so restrictive in what he regarded as a "positive" family history. It has to be remembered that sudden deaths or strokes are not always associated with hypertension—especially in subjects aged over sixty years. The present estimate is probably an over-estimate, but it must be nearer the true incidence of hypertensive vascular disease than an estimate based on Platt's criteria. If every possible relative with vascular disease had been included the figure would be 44% of "positive" findings, so there is a considerable discrepancy between the two findings.

Undue social or financial difficulties were found in 30% of these cases—22% among the men, but 36% among the women. The significance of this finding is difficult to assess in the hospital population.

Obsessional compulsive personality traits were prominent in 50% of the patients of both sexes. In men they took the form of great conscientiousness and punctiliousness in many cases. The subjects were often skilled tradesmen, foremen or business men. They usually had positions of responsibility and were leaders of their groups. In women, over-anxiety and a strong urge to keep their houses spotless were found. Similar findings in a carefully controlled study are reported by Gressel *et alii* (1950).

This finding is regarded as more significant than the presence of undue stress in the environment. It may indicate a constitutional factor which is of considerable importance in the management of treatment, for these patients often cannot relax when it is in their interests to do so for the sake of their health.

Obesity was common in women (42%) but rare in men (5%).

Evidence of endocrine imbalance, such as hirsutism, and some evidence suggestive of myxœdema or thyreotoxicosis were found quite commonly in the women (34%) but not at all in the men. It is interesting to note that there were only three diabetics in the whole series.

It may be added that little evidence of any of these factors was found in patients suffering from renal hypertension.

Pregnancy Toxæmia.—A history of toxæmia of pregnancy was given by no less than 47 of 106 women in the series with primary or essential hypertension; this figure represented 53% of the parous women with primary hypertension. In addition a history of toxæmia of pregnancy was found in three cases of renal hypertension.

It has been found that the women with a history of toxæmia of pregnancy were younger than those without such a history. There were 31 out of 47 patients with a history of toxæmia aged forty years or less, while of those without a history of toxæmia only 12 out of 59 were in this age group. This difference was statistically significant ($P<0.001$). In no fewer than 39 of these 47 cases, or 83%, the hypertension persisted following either true toxæmia (24) or so-called hypertensive toxæmia of pregnancy (15). It would appear that the toxæmia of pregnancy either initiated the disease or brought it on earlier than it would otherwise have appeared. A "positive" family history was less common in these cases (35%) than in those without a record of toxæmia of pregnancy (63%). It was also of interest to find that 68% of these patients showed obsessional traits, in contrast to 39% of those without a history of toxæmia of pregnancy.

These women were a remarkably homogeneous group from the point of view of physical and mental make-up. They tended to be short and stout, with flushed faces, clammy hands and lustreless hair. They became excited very easily—for example, at the sight of a white coat in the ward some distance away. This excitement was often accompanied by a pronounced vasomotor reaction with flushing of the face and neck and perhaps sweating. The picture is somewhat suggestive of thyreotoxicosis—a diagnosis which would find support in the elevated basal metabolic rate which has been found very common (90%) in these women. This clinical picture is reminiscent of the diencephalic syndrome described by Page (1935) in patients with essential hypertension.

Only three patients over the age of fifty years with a history of toxæmia of pregnancy were seen. This could be due to various factors, but the most likely explanation

TABLE II.

Factors Associated with Primary Hypertension.

Sex.	Family History.	Stress Present.	Personality Traits.	Obesity.	Endocrine Disturbance.	Total Number in Class.
Male	14	16	35	4	—	74
Female	46	38	55	44	36	106
Total	60	54	90	48	36	180

would appear to be that these patients generally do not live so long, for almost half (41%) of the patients already had serious complications. This is in comparison with 61% of serious complications in women without a history of toxæmia of pregnancy (see Table III). Hence the prognosis in this class of case would appear to be more serious.

Hypertensive Vascular Disease.

The complications of hypertension are due to hypertensive vascular disease—a disease affecting the arterioles throughout the vascular tree and not just those of the kidney, as was once thought. This diffuse arteriolar disease (Wagener and Keith, 1939) produces effects in every organ, but particularly in heart, brain, kidney and retina. The syndrome of malignant hypertension represents the fully developed clinical picture of diffuse arteriolar disease. In clinically significant non-malignant hypertension the condition is not so well developed, but there is nearly always evidence of it in more than one organ or system, unlike atheroma, which usually produces signs and symptoms from only one organ.

The *fundi oculorum* provide the only arterioles which can be seen directly, and ophthalmoscopic examination gives a good indication of the extent of diffuse arteriolar disease in any case of hypertension. Castleman and Smithwick (1943, 1948) found a good correlation between the condition of retinal arterioles and renal arterioles. In this series of 203 patients the following evidence was found: 10% had irregular and thin calibre arterioles; 10% had irregular calibre arterioles with nipping of veins; 10% had irregular calibre arterioles with arterio-venous nipping, hæmorrhages and exudates; 25% had the fully developed picture of retinal œdema discussed more fully under the malignant hypertension syndrome.

The incidence of the various complications apart from retinal damage is shown in Table III.

The greater severity of the disease in males is indicated by the comparatively few cases (16%) with headache as their main presenting symptom, in contrast to the females (45%). Malignant hypertension, in accordance with general experience, is much more common in males (49%) than in females (11%). All the other complications, with the exception of angina of effort, are also more common in males. Angina of effort is seen to be very uncommon in association with hypertensive vascular disease. Uræmia—that is, death with a blood urea nitrogen level greater than 100 milligrammes *per centum*—is also uncommon. In the cases of secondary hypertension, 14 of the 22 patients developed the complication of malignant hypertension.

There were four females and three males in this series who were symptomless. In three other cases the symptoms were not attributable to hypertension.

Common Manifestations.

The following manifestations of hypertensive vascular disease will be considered in detail: (i) malignant hypertension, (ii) hypertensive heart disease, (iii) hypertensive cerebral disease, (iv) hypertensive renal disease.

Malignant Hypertension.—In accordance with the work of Ellis (1938), malignant hypertension has been diagnosed whenever papillœdema has persisted with chronic hypertension. Papillœdema is seen occasionally in association with hypertension accompanying acute nephritis and toxæmia of pregnancy—that is, as a result of rapidly rising blood pressure—but it subsides again with the subsidence of the hypertension. In chronic hypertension papillœdema is usually associated with evidence of widespread vascular damage (diffuse arteriolar disease) in the heart, brain and kidneys, apart from the retina. On pathological examination fibrinoid necrosis is usually found in the arteriolar walls—a condition similar to that found by Wilson and Byrom (1939) in rats with severe hypertension. It has been found that these clinical and pathological findings are the result of hypertension irrespective of its cause—primary, renal or endocrine (Derow and Altschule, 1941). The condition of malignant hypertension should therefore be regarded as a syndrome and not as a specific pathological entity. Ellis (1938), however, has suggested that the term be reserved for primary malignant hypertension, and it is often restricted to this group of cases. But it should be realized that there is no clinical or pathological justification for this division, and a division into two groups, primary and secondary malignant hypertension, would seem to be more useful and will be used in this paper.

There were 36 cases of primary malignant hypertension and 14 of secondary malignant hypertension in this series. All the secondary cases were due to renal disease, which indicates how commonly the condition occurs as a complication of renal hypertension.

Only 10 of the patients with primary malignant hypertension (eight men and two women) were aged over fifty-five years. All the patients with secondary malignant hypertension were aged under forty years. Only six (three male and three female) patients with primary malignant hypertension had their condition diagnosed under the age of forty years. This confirms the experience of Platt (1948), who found primary malignant hypertension very uncommon under the age of forty years. In his series of 64 cases Platt found 7·8%; in this series of 60 cases there were 10%.

The presenting symptom in these cases is either dyspnœa or visual upset. There may be a history of hypertension of up to ten years' duration, although it is not usually of more than five years' duration. Examination discloses evidence of left ventricular failure with gallop rhythm very frequently, and papillœdema.

The appearance the fundus presents is not the same as in papillœdema due to intracranial tumour with increased intracranial pressure. First of all the disk margins are obviously blurred, but this blurring is not associated with obliteration of the vascular reflex of the vessels travelling over the disk, as is so commonly the case in classical

TABLE III.

Incidence of Main Complications of Hypertension.

Subjects.	Malignant Hypertensive Syndrome.	Congestive Cardiac Failure.	Angina of Effort.	Cerebro-vascular Accident.	Hypertensive Encephalo-pathy.	Uræmia.	Headache.	Total.
Males	24	17	—	12	4	2	11	70
Females:								
History of pregnancy toxæmia	4	9	2	3	2	—	24	44
No history of pregnancy toxæmia	8	13	2	8	4	—	22	57
Total	12	22	4	11	6	—	46	101
Primary total	36	39	4	23	10	2	57	171
Secondary total	14	2	—	—	—	2	4	22
Grand total	50	41	4	23	10	4	61	193

papillœdema due to intracranial tumour. The condition therefore seems to be more general retinal œdema than localized œdema of the disk, and it has been seen to cause retinal detachment in at least two cases in this series.

In association with this appearance there is usually evidence of gross vascular damage—pronounced nipping or obliteration of the vessels at the arterio-venous crossings. The veins are usually engorged and there are extensive hæmorrhages and exudates. Of particular interest, however, is the fact that the arterioles are nearly always very hard to see. This appears to be more likely to be due to severe vascular spasm than to obliteration by œdema.

TABLE IV.

Cerebro-spinal Fluid Pressure in Twenty Cases of Hypertension with Retinal Œdema (Grade IV Retinitis).

Cerebro-spinal Fluid Pressure. (Millimetres of Water.)	Number of Cases.
80 to 180	7
180 to 240	7
245 to 500	6
Total	20

The retinal œdema loosely called papillœdema is usually ascribed to increased intracranial pressure (McAlpine, 1933), so it was of interest to investigate the cerebro-spinal fluid pressure in these cases. The findings in a series of 20 cases are shown in Table IV. The figures do not support the contention that this retinal œdema is due to increased intracranial pressure. The presence of congestive cardiac failure must have assisted considerably the elevation in three of the cases in which the highest pressures were recorded.

It appears much more likely that this change is the result of vascular damage. In keeping with this view is the occurrence of unilateral or unequal changes in the two eyes. The remarkable improvement of the retinal condition seen following sympathectomy irrespective of a fall in blood pressure rather points to a reversible or spastic element in the condition. It seems probable that a raised cerebro-spinal fluid pressure will occur once there is a certain degree of œdema throughout the brain resulting from extensive vascular damage.

The course in malignant hypertension was short irrespective of the cause. In the primary group at least 17 of the 24 men are dead and six of the 12 women. Generally death occurred within a few months of their first admission to hospital. In the secondary group 11 out of 14 are already dead.

Death is often attributed to uræmia in these cases, but cardiac failure is nearly always a prominent feature of the clinical picture. Table V gives an analysis of the main features in 49 of these cases.

It will be seen that death is most commonly due to cardio-renal failure, a combination of congestive failure with a moderate elevation of the blood urea nitrogen level (approximately 50 milligrammes *per centum*). Death has been attributed to uræmia when the blood urea nitrogen level has reached 100 milligrammes *per centum*, but even in these cases left ventricular failure was usually the presenting condition. Pericarditis was found terminally in just under half of these cases of malignant hypertension in which death was due to cardio-renal or renal failure.

Professor J. S. Robertson of the University of Adelaide (Robertson, 1951) has carefully examined sections taken from many parts of the vascular tree in some of these cases. He was able to find areas of fibrinoid necrosis in most of the cases irrespective of whether the subjects had suffered from primary or secondary hypertension. A good correlation with the clinical diagnosis based on the presence of retinal œdema was obtained. The work of Byrom and Dodson (1948) would suggest that the presence of these lesions depends on the amount of mechanical strain to which the vessels are exposed. This may in turn depend on the height of the blood pressure and the rapidity of its fluctuations.

Hypertensive Heart Disease.—Occurring in association with either malignant or non-malignant hypertension, hypertensive heart disease is the commonest clinical complication of hypertensive vascular disease next to retinal damage. Congestive cardiac failure (usually of left ventricular type) had occurred in nearly one-third of the cases in the series. Presenting with dyspnœa, followed by enlargement of the heart and "gallop" rhythm, the condition is usually progressive and leads to death usually within two years.

Harrison and Wood (1949) have directed attention to the clinical differences between hypertensive heart disease and "ischæmic" heart disease resulting from coronary disease. In contrast to the progressive course of the former is the good temporary recovery with abrupt death characteristic of the latter. In the former there is usually evidence of hypertensive vascular disease elsewhere—for example, in the retina, brain or kidney—whereas in the latter the disease is usually localized in the heart.

Cassidy (1946) found that 42·3% of his 1000 patients with coronary disease had blood pressures between 160 and 200 millimetres of mercury (systolic) and 100 and 120 millimetres (diastolic), 30·6% had normal blood pressure, and 27·1% had blood pressure greater than 200 millimetres of mercury (systolic) and 120 millimetres (diastolic). He suggested on the basis of these figures that hypertension and coronary disease may have a common ætiological factor. But 87% of his male patients and 82% of his female patients were aged over fifty years. It would appear, therefore, in the light of the findings of Master *et alii* (1943), that what he called "moderate hypertension" was not much more frequent than would be found in a random sample of the population aged over fifty years. Therefore, significant hypertension occurred only to the extent of 27·1%—a not very high proportion of his cases of coronary disease.

Comparison of the age incidence of hypertensive vascular disease with complications such as malignant hypertension, congestive cardiac failure or cerebro-vascular accident in this series shows a highly significant difference from a series of patients admitted with myocardial infarction to the Royal Adelaide Hospital over the same period. Only 18% of these latter were aged under fifty years, while nearly half (45%) of the hypertensive group were aged under fifty years.

We have already noted the low incidence of angina of effort in the hypertensive series. Clinical or electro-

TABLE V.

Malignant Hypertension Syndrome.

Type.	Cardio-renal Failure.	Congestive Cardiac Failure.	Cerebro-vascular Accident.	Uræmia.	Headache.	Total.
Primary ..	9	10	8	5	4	36
Secondary ..	8	1	—	3	1	13
Total	17	11	8	8	5	49

cardiographic evidence, or both, of coronary disease was found in a total of only 14% of the patients in the series aged more than forty years, and it may well have been due to coincident atheroma in these cases. However, more than one-third of the patients showed the pattern of so-called "left ventricular strain" (low *S–T* segment with an inverted *T* wave in the limb leads). Enlarged heart found on X-ray examination was somewhat less common than the "left ventricular strain" finding, but in practically every case in which an enlarged heart was found radiologically there was evidence of the "left ventricular strain" pattern. In a few cases "left ventricular strain" was found without evidence of cardiac enlargement—a finding which Leishmann (1951) suggests may be due to impaired coronary circulation, and therefore of more serious prognosis than those cases in which it is associated with enlarged heart, when it probably simply reflects the increased size of the muscle fibres.

Hypertensive Cerebral Disease.—Only six patients in the series had intracerebral hæmorrhage, and these cases were all fatal. Other patients were admitted to hospital with the condition over the period during which this series was collected, but they died soon after admission. Five other patients had subarachnoid hæmorrhages; two of these died from recurrences within a fortnight.

Apart from these conditions, the cerebro-vascular seizures were nearly all mild, with rapid recovery in two-thirds of the cases. There does not seem to be any definite division between attacks labelled "cerebral thrombosis" and those labelled "hypertensive encephalopathy" (Oppenheimer and Fishberg, 1928). This has also been found by Pickering (1948), who adduces this as evidence in favour of a single cause for all—namely, organic arterial obstruction.

McAlpine (1933) classified hypertensive encephalopathy into (i) the œdematous type, characterized by headache, and papillœdema due to cerebral œdema with increased intracranial pressure occurring in patients aged under forty years, and (ii) the dry type (due to spasm) characterized by focal seizures and convulsions in patients aged over forty years. However, study of the cases of hypertensive encephalopathy in this series indicates that this clinical division is not a very sharp one, for papillœdema occurs often in patients aged over forty years, especially in malignant hypertension, while focal seizures and convulsions are quite common in patients aged less than forty years with evidence of cerebral œdema.

These observations would suggest that the two types of encephalopathy may not be so different as was once thought. Clinically the condition of the actual nerve head in malignant hypertension (*vide supra*) suggests that focal œdematous areas caused by vascular damage can occur in human hypertension, while the rapid improvement following sympathectomy (independent of a general fall in blood pressure) points to a reversible and possibly spastic element in the condition. Subsequent thrombosis in a spastic vessel may determine the ultimate course.

Hypertensive Renal Disease.—Albuminuria occurred in 20% of the cases of primary hypertension. A defective result of the urea concentration test (inability to attain 2% in any one specimen) occurred in 18% of the cases. More advanced deterioration of renal function as indicated by urea clearance tests is uncommon in primary hypertension (seen only in two cases) until it enters the malignant phase. Death in uræmia in primary hypertension will be seen to be uncommon even in the malignant cases (Table V), although cardio-renal failure is the usual termination of malignant hypertension whether it is of primary or secondary (renal) origin.

General Discussion.

A number of investigations have been made into the natural history of hypertensive vascular disease following the pioneer observations of Bright (1827), Johnson (1868), Gull and Sutton (1872), and Allbutt (1896). One of the first was that of Janeway (1913), who reported a five to ten year follow-up of 458 private patients with a systolic blood pressure greater than 160 millimetres of mercury. The average duration of life after the first symptoms had appeared proved to be four years in men and five years in women, although 25% lived more than ten years. Janeway emphasized the importance of the effects on the heart; but the value of his paper is lessened by the fact that renal hypertension was not recognized as a special type of hypertension until after the work of Volhard and Fahr (1914) had appeared. Janeway's initial observation that many hypertensive patients might live for many years in good health was subsequently confirmed by Ehrström (1918).

These reports of the good prognosis for patients with hypertension are confirmed by the prevalence of mild hypertension in a representative sample of the "normal" population discovered by Master *et alii* (1943), who found that more than half of those aged over forty-five years had blood pressures greater than 150 millimetres of mercury (systolic) and 90 millimetres (diastolic).

In this series, on analysis, the blood pressure readings showed the following figures. All 203 patients had blood pressures greater than 160 millimetres of mercury (systolic) and 100 millimetres (diastolic), 26 had blood pressures less than 180 millimetres of mercury (systolic) and 120 millimetres (diastolic), of whom 20 were aged less than fifty years (six men and 14 women). In the other cases (subjects aged over fifty years) complications were present. The levels found indicate that in 90% of the cases hypertensive disease severe enough to be associated with complications and to warrant admission to hospital for treatment is associated with a level of blood pressure of 180 millimetres of mercury (systolic) and 120 millimetres (diastolic), or higher.

This finding is complemented by those of Bechgaard (1946) and of Burgess (1948). Bechgaard (1946) found in his four to eleven years follow-up of 1038 patients that the diastolic pressure had to be 120 millimetres of mercury in men and 130 millimetres in women (systolic, 200 and 230 millimetres respectively) before there was a significant increase in mortality. Burgess (1948), in his twenty-years follow-up of 100 patients, found that hypertension was not associated with significant shortening of life unless it had appeared before the age of fifty years and the diastolic pressure was 120 millimetres of mercury or more. The good prognosis of hypertension in women has been emphasized by Perera and Blood (1948). All these findings refer, of course, to "primary" or "essential" hypertension, and they would suggest that such hypertension is not clinically significant until this level of diastolic pressure is reached. The experience of this series would support this contention.

These findings offer strong support for the approach to normal blood pressure adopted by Master *et alii* (1950). This approach is in contrast to that of insurance statistics —for example, that of Robinson and Brucer (1939). The latter workers have fixed a level, 140 millimetres of mercury (systolic) and 90 millimetres (diastolic), above which it is stated that life expectancy is shortened at any age. There is, however, no adequate allowance for age or sex in the figure, because the insurance companies are primarily concerned with men aged below forty years. On these criteria hypertension is more common than normal blood pressure in persons aged over forty-five years (Master *et alii*, 1943).

However, Master *et alii* (1950) have based their normal figures on a statistical definition. First of all, the average blood pressure has been calculated from a large sample (15,706 persons—civilians: 7722 male and 7984 female), and then, by the use of current statistical procedure, the 95% probability limits are worked out. This range has been calculated for different ages, and any levels outside these limits are regarded as being probably abnormal although not necessarily so.

Master *et alii* (1950), using this approach, found a wider range of normal blood pressure for the different ages than has previously been put forward; but their limits (up to 170 millimetres of mercury, systolic, and 110 millimetres, diastolic, at sixty-four years) appear to conform more with the clinical experience of this series and with those of Bechgaard (1946) and Burgess (1948). The calculations are based on the reasonable assumption that blood pressure

readings (like other biological populations) are normally distributed, and are more useful for individual cases than the means of large groups taking no account of age or natural variation.

It is suggested, therefore, that clinically significant hypertension should not be diagnosed in patients aged over forty years unless the diastolic blood pressure has reached 120 millimetres of mercury when taken under properly controlled conditions. An elevation of less severe degree is usually due to arteriosclerosis, as part of the aging process in western civilization, and is not itself a factor in shortening life expectancy.

As has been indicated above, these considerations are very important in evaluating the findings of Cassidy (1946) on the significance of hypertension in association with coronary disease, and also the findings of Platt (1947) in relation to the incidence of a family history of hypertension in patients suffering from essential hypertension.

The most interesting finding from the ætiological point of view is the high incidence of obsessional compulsive traits in the personality of these patients. This was apparent even in those women with a history of toxæmia of pregnancy, which may imply that these patients may have developed hypertension in any case, as was originally suggested by Browne and Dodds (1939) from other evidence.

The development of such traits is probably a reaction to the exigencies of our modern life, for the evidence reviewed by Smirk (1949) on the incidence of hypertension among people of different races and environments would suggest that primary hypertension develops in certain predisposed individuals as a result of present conditions of living in western civilization. The nature of this predisposition has been investigated by Wolf *et alii* (1948) and by Pfeiffer and Wolff (1950), and evidence has been produced that hypertensive patients respond to everyday stresses with a protective reaction pattern involving the vascular system, particularly the renal circulation.

Summary and Conclusions.

The clinical features of a series of 203 patients with hypertension are reviewed in an attempt to define more clearly the nature of the clinical problems associated with the condition. The main conclusions are as follows.

Ætiology.

The known causes of hypertension accounted for only 11% of the cases. An investigation was made into some of the factors associated with the cases of "primary" or "essential" hypertension which comprised 89% of the cases in the series.

In men obsessional compulsive personality traits were found in 50%, but there was little evidence of obesity or endocrine disturbance. Family history was positive in only 19%.

In women a history of toxæmia of pregnancy occurred in 53% of those who were parous, and in 83% of these cases the hypertension dated from pregnancy. Evidence of compulsive personality traits was present in 50%; a "positive" family history was present in 43%.

The general conclusion on ætiology is that "essential" hypertension is probably caused by a particular protective reaction pattern to the everyday stresses of modern western civilization—a pattern which involves the vascular system.

Course.

The course of a case of hypertension is determined by the development of hypertensive vascular disease, which is characterized by diffuse arteriolar disease. "Primary" hypertension which is clinically significant appears by the age of fifty years, the blood pressure reading being at least 180 millimetres of mercury (systolic) and 120 millimetres (diastolic).

In "primary" hypertension the course is more rapid in men than in women. In women the course is more rapid in those who have had an episode of toxæmia of pregnancy.

The condition termed malignant hypertension is the most advanced stage of hypertensive vascular disease. It is indicated clinically by diffuse retinal œdema called "papill-œdema", which is not produced by increased intracranial pressure but by vascular damage. This complication is especially frequent in renal hypertension and is responsible for its bad prognosis.

Atheromatous vascular disease has quite distinct clinical manifestations from hypertensive vascular disease. In contrast to the latter, it produces effects after the age of fifty years, and is associated with only mild hypertension —less than 180 millimetres of mercury (systolic) and 120 millimetres (diastolic). The prognosis depends on the local arterial disease and not on the hypertension.

Acknowledgements.

The writer wishes to express his thanks to Dr. F. Ray Hone for the initial encouragement which led to this work. The help of the Director of the Institute of Medical and Veterinary Science, Dr. J. Orde Poynton, and of Dr. C. C. Jungfer was invaluable in the planning of the investigation. The writer is also indebted to the honorary and resident medical staffs of the Royal Adelaide Hospital for their ready cooperation.

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AN ACRYLIC SPLINT FOR THE ARTHRITIC HAND.

By MICHAEL KELLY,
Melbourne.

IN early rheumatoid arthritis we are often confronted with a woman whose painful and swollen metacarpo-phalangeal (basal) joints incapacitate her by day and keep her awake at night.

Noticing her fingers becoming stiffer, she practises indiscriminate exercises, which further damage the inflamed joints. As the arthritic process advances, the sheaths of

FIGURE I.
Arthritis of metacarpo-phalangeal joints. Position on attempting to close hand.

the flexor tendons become sticky where they cross the palmar aspects of the basal joints. If the tendons become adherent, the interphalangeal joints cannot be flexed; she can grasp only with straight fingers, hyperflexed at the basal joints (Figure I). These later become subluxated; if the joint of the little finger is involved, ulnar deviation follows.

When the patient can no longer use her hands she moves her arms less and less. The wrists droop and the forearms are pronated, and the humeri are kept adducted.

If the stiffening of the interphalangeal joints can be prevented, the patient will continue to use her hand and the other joints will not become fixed. Active movement of the basal joints is harmful; they therefore must be held in extension while the middle and distal joints are exercised. With continuous immobilization by plaster the

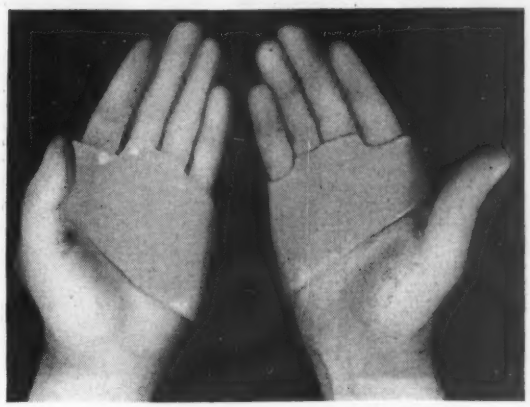

FIGURE IIA.
Acrylic splints applied for arthritis of metacarpo-phalangeal joints of both hands. (Splints should be bored with holes all over.)

arthritic process subsides and the long tendons begin to move again (Kelly, 1950). Pain in the hands, and sometimes in the shoulders and other distant joints, is relieved and the general health improves remarkably.

More recently a removable plaster splint, well dried and coated with lacquer, has been used for intermittent wear. Better still, the plaster cast can be used as a model for an

FIGURE IIB.
Same case as in Figure IIA. Acrylic splints applied for arthritis of metacarpo-phalangeal joints of both hands. Middle joints cannot yet be completely flexed.

acrylic splint, which can be worn continuously and is not damaged by water. The splint should not interfere with thumb movements and it should allow full flexion of the middle joints of the fingers; thus it should terminate at the middle of each proximal phalanx, not more than half an inch beyond the web (Figures IIA and IIB). Where severe ulnar deviation has to be corrected, the splint may extend to the distal joint of the little finger (Figures IIIA and IIIB). It should be bored with holes all over to allow evaporation of sweat (this is not shown in the figures).

The splint should be worn through the night and as much as possible during the day. It allows use of the hands for most tasks; it is easily slipped on and off. Even in old-standing cases a fair amount of flexion can be restored to interphalangeal joints by assiduous flexion exercises under control by the splint. A busy housewife can be persuaded thus far, but she cannot easily be persuaded to wear appliances which aim to restore movements by elastic traction or by spring pressure.

FIGURE IIIA. FIGURE IIIB.

Acrylic splint applied for advanced arthritis of metacarpo-phalangeal and interphalangeal joints, with ulnar deviation. Splint extends to distal joint of little finger.

Summary.

A removable acrylic splint is described which, by fixing the metacarpo-phalangeal joints of the fingers and allowing full flexion of the phalangeal joints, relieves pain and prevents stiffness and deformity in arthritic fingers.

Acknowledgements.

My thanks are due to Mr. C. Wellington, of the facio-maxillary unit, Royal Melbourne Hospital, for making the splints; to Mr. Inglis, for expert photography; and to Dr. R. Howden, for permitting me to treat patients at the arthritis clinic.

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Reviews.

PSYCHIATRY FOR THE LAITY.

ACCORDING to its dust-cover, "How Psychiatry Helps", by Phillip Polatin and Ellen C. Philtine, "belongs to the top of the best selling list".[1] It is a debatable point whether it is desirable for any branch of medicine to advertise its wares in the popular Press, and we cannot agree that it is any more necessary for psychiatry to do so, even though "an unusually large number of psychiatric books for the laymen, filled with verbal champagne, inspirational phrases and sociological ruminations have appeared since the last World War". For all that the authors make a valiant attempt to achieve their purpose, which appears to be to give to laymen a bird's-eye view of all the techniques and drugs used in psychiatry With such an object in view and for such an audience, the material is naturally rather uncritically presented and very much over-simplified. The uninformed reader will be likely to form much more grandiose and optimistic opinions of the outcome of psychiatric treatment than are justified in fact.

The scope of the book includes brief glances at all recognized forms of psychotherapy, psychosomatic medicine, "shock treatment" (*sic*), psychosurgery, chemical treatments (including truth serum!) and other treatments for specific illnesses including epilepsy and general paresis. A medical practitioner would be wise to read the book before recommending it to a patient.

[1] "How Psychiatry Helps", by Phillip Polatin, M.D., and Ellen C. Philtine, with a foreword by Nolan D. C. Lewis, M.D.; 1951. Kingswood, Surrey: The World's Work, Limited. 7¼" × 5", pp. 262. Price: 10s. 6d.

THE INTRAVENOUS USE OF PROCAINE.

D. J. GRAUBARD and M. C. PETERSON[1] have treated many disorders by the slow intravenous infusion of procaine. Their experience in 4000 cases of traumatic and inflammatory diseases and poliomyelitis is summarized in a small volume; introductory chapters describe the pharmacology of procaine and Bier's method of intravenous renal analgesia. In the remaining chapters the authors discuss the experiences of others with the intravenous use of procaine for such widely divergent disorders as pruritus, serum sickness, burns, post-operative pain, cardiac arrhythmias during anæsthesia, labour pains, pulmonary embolism, anuria, glaucoma, retinal detachment, frostbite, asthma, infantile gastro-enteritis and eclampsia. A bibliography—complete to 1948—is provided, but the book lacks an index. The authors state that there are no contraindications except individual susceptibility to procaine. The rate of infusion should be adjusted to keep the procaine level in the blood at 0·04 milligramme per millilitre. The authors have had no serious complications in 4000 infusions; two patients lost consciousness momentarily. Some writers since 1948, however, have reported negative results and unfavourable effects, and even deaths.

In regard to disorders which are subject to fluctuations and to remission of symptoms, claims for benefit from new therapeutic procedures should be scrutinized with care. In this book we look in vain for control series and for evidence that the conclusions of the authors have been subjected to critical analysis.

[1] "Clinical Uses of Intravenous Procaine", by David J. Graubard, M.D., and Milton C. Peterson, M.D.; British Commonwealth Edition, edited by William W. Mushin, F.F.A., R.C.S., D.A.; 1951. Oxford: Blackwell Scientific Publications. 8½" × 5½", pp. 96. Price: 8s. 6d.

INCONTINENCE IN THE AGED.

A STUDY of one of the most difficult nursing problems in geriatrics is described in John C. Brocklehurst's "Incontinence in Old People".[2] The growing importance of the subject is emphasized by the fact that in Britain the proportion of the population over sixty-five years will increase from 4·8% in 1881 to 18·6% in 1979. "Its seriousness today is but a portent of what is to come unless we can make of old age a happy and fruitful part of life."

The first part of this monograph consists of a review of the anatomy and physiology of the bladder and rectum, of the mechanics of micturition, of nervous diseases and of the pharmacology of adrenaline, ephedrine and trasentin as they affect these organs.

Two surveys were made—first, of the main Glasgow hospitals which had special provision for the elderly, and second, in more detail of one hundred cases of incontinence. From these some of the notable conclusions are the following.

Organic nervous disease occurs equally in the continent and incontinent, but hemiplegia is more frequently associated with incontinence. One-third of the incontinent patients have some organic nervous lesion and one-third suffer from mental confusion. Women are twice as susceptible as men, but both child-bearing and enlargement of the prostate are of minor importance ætiologically. The main predisposing cause is a lesion of the central nervous system, especially cortical or between the cortex and a tonic motor centre. Incontinence is precipitated by a cerebro-vascular accident, by increasing confusion or by the patient becoming bed-fast.

[2] "Incontinence in Old People", by John C. Brocklehurst, M.D., with a foreword by Stanley Alstead, M.D., F.R.C.P.; 1951. Edinburgh: E. and S. Livingstone, Limited. 10" × 7", pp. 204, with 62 figures. Price: 30s.

Management is considered mainly from the institutional viewpoint. Rightly, rehabilitation is of prime importance, particularly if the individual can be made ambulant. Only a small proportion of patients respond to drugs and some of the more cooperative can use an improved variety of urinal. To facilitate nursing, to prevent bed sores and to conserve linen, much ingenuity has been expended in the devising of special beds for the incontinent. The current model is of wooden laths covered with sponge rubber on a frame which fits the usual iron bedstead. However, this involves long periods of immobility which only a limited number of patients will tolerate.

This book is very well produced, with good illustrations and clear print on excellent paper. The subject is one of great interest to all practitioners who deal with the aged, and the surveys and recommendations in this book should be carefully considered by those concerned with the institutional care of the aged.

A YEAR BOOK OF PATHOLOGY AND CLINICAL PATHOLOGY.

FOLLOWING his established practice, the editor of the section on pathology in "The 1950 Year Book of Pathology and Clinical Pathology", Howard T. Karsner, has included a number of short special articles by invited contributors, each on a subject with which the contributor's name has been especially associated.[1] Of most general interest is Hans Selye's summary of his work and views up to January, 1951, on the general adaptation syndrome and diseases of adaptation, but many readers will welcome also the article by W. Barry Wood, junior, on the role of surface phagocytosis in acute bacterial infections and that by Berta Scharrer on tumours in invertebrates. The rest of the abstracted material in this section is grouped into chapters on general pathology, the cardio-vascular, hæmopoietic and respiratory systems, the alimentary tract and associated glands, the urinary system and male genitalia, the female genitalia and breast, glands of internal secretion, the nervous system and miscellaneous subjects. The editor has included a report by J. A. Inglis and J. I. Tonge, of Brisbane, of a disease with visceral granulomatous lesions of unknown origin and a paper by E. S. J. King, of Melbourne, on the genesis of varicose veins.

The section on clinical pathology has chapters on hæmatology, chemistry, bacteriology, mycology, serology, parasitology, allergy and endocrinology, cytology, microscopy, apparatus and statistics. A good deal of the material is of a practical nature and presented at sufficient length to allow inclusion of details of tests, technical procedures and the like. In an introduction the editor, A. H. Sanford, refers briefly to the history of clinical pathology in the past fifty years and reviews the advances of the decade 1940-1950.

Like all the Practical Medicine Year Books the volume is admirably produced. It is an important publication for pathologists, bacteriologists and their scientific kin, to whom some of the material will be of exclusive interest. It will be welcomed also by many physicians, general practitioners and others who realize the value of keeping their basic medical knowledge up to date.

"ADDENDUM 1951 TO THE BRITISH PHARMACOPŒIA 1948."

THE comparatively recent practice of publishing periodical addenda to the current British Pharmacopœia is a wholesome attempt to bring it more continuously into alignment with advances in therapeutics and the ancillary sciences and to minimize the unavoidable lag between pharmacological progress and its pharmacopœial acknowledgement.

The present Addendum[2] assumes official status in Great Britain from September 1, 1951, and has the same authority as the British Pharmacopœia with regard to new monographs, while amended monographs and appendices supersede the originals in the British Pharmacopœia 1948. Its official adoption in Australia will be at a later date, yet to be proclaimed.

Perhaps the most outstanding innovation is a section devoted solely to preparations of human blood. This includes monographs on whole blood, concentrated red blood corpuscles, fibrin foam, fibrinogen, dried plasma, thrombin and liquid and dried serum.

While in the early proofs of the Addendum these products were listed under somewhat cumbersome Latinized titles, the Commission has, with exemplary courage, broken the tradition of a century of pharmacopœial nomenclature by discarding Latin titles in favour of their English names. With linguistic inconsistency, we shout *"bravissimo"* to this innovation and hope to see it spread, in due course, to all the monographs.

The Latinizing of the names of newer medicaments—for example, *Procainæ Benzylpenicillinum*—and of many biological products such as *Tuberculini Derivatum Proteinicum Purificatum*—enshroud these products with an aura of unreality and can be regarded only as a concession to a practice that has outlived its usefulness.

The antibiotics are well represented by penicillin G, the streptomycins and chloramphenicol, but aureomycin has not yet received official cognizance. Crystalline penicillin G (*Benzylpenicillinum*) in the form of the sodium and potassium salts is differentiated from the penicillinum, British Pharmacopœia 1948, which represents the sodium and the calcium salts of the mixed and less refined antimocrobial acids of *Penicillium notatum*. It is also available as the procaine salt (*Procainæ Benzylpenicillinum*) and it is to be noted that when procaine penicillin is prescribed, the official benzylpenicillin salt must be supplied.

The standard strengths of penicillin in the creams and ointment have been increased to 1000 units per gramme, while, for the ointment, the erstwhile wool-alcohols base is replaced with a paraffin mixture. A change from an oil-miscible base seems to have been indicated, but, for efficient delivery of the antibiotic to wounds or to exudative skin lesions, one would have expected the change to favour a potentially water-miscible hydrophilic base.

The streptomycins comprise the hydrochloride, the sulphate and the calcium chloride complex as well as salts of dihydrostreptomycin. It is to be noted that when streptomycin is ordered without further specification, the calcium chloride complex will be dispensed.

No guidance is given as to the dosage of these antibiotics, this being "determined by the physician in accordance with the needs of the patient". While appreciating the difficulties in enunciating appropriate dosage for these and certain other drugs, we rather think that some guidance should be given, not only for the benefit of the prescriber and the dispenser, but as a basis for teaching purposes. This applies particularly to other more immediately toxic drugs—notably in this Addendum, tubocurarine and dimercaprol (BAL)—where, at least, some indication of the upper limits of therapeutic tolerance should certainly be supplied.

Several bacterial vaccines, notably those of cholera, whooping-cough, plague and the typhoid-paratyphoid group, have been brought up to date with regard to specification of the particular types and strains of bacteria used, and modes of culture and preparation, together with details of specific antigens in each. Typhoid-paratyphoid A, B and C vaccine has been added, and, in the case of the typhoid-paratyphoid group, alcohol treated vaccines are included.

Minor amendments have been made in the monographs dealing with the antitoxins. The international unit, 1950—equivalent to two international units, 1928—has been adopted for tetanus antitoxin. Mixed gas gangrene antitoxin (*Antitoxinum Oedematiens Co.*) is renamed *Antitoxinum Gasgangrœnosum Co.*

Many of the complex organic drugs, now included, are well known in everyday practice, and some have already appeared in the British Pharmaceutical Codex 1949. The antihistamines are represented by mepyramine maleate and promethazine hydrochloride—more familiar under their proprietary names of "Anthisan" and "Phenergan" respectively.

To the increasing lists of barbiturates and sulphonamides are added quinalbarbitone sodium ("Seconal Sodium") and sulphadimidine.

[1] "The 1950 Year Book of Pathology and Clinical Pathology (January-December, 1950); Pathology, edited by Howard T. Karsner, M.D., LL.D., Clinical Pathology, edited by Arthur Hawley Sanford, M.D.; 1951. Chicago: The Year Book Publishers, Incorporated. 8" x 5¼", pp. 456, with 157 illustrations. Price: $5.00.

[2] "Addendum 1951 to the British Pharmacopœia 1948", published under the direction of the General Medical Council pursuant to the *Medical Council Act*, 1862, and the *Medical Act*, 1950. London: Published for the General Medical Council by Constable and Company, Limited. 8¼" x 3¾", pp. 132. Price: 17s. 6d.

Proguanil hydrochloride ("Paludrine") as an antimalarial is included, but chloroquine and pentaquine have not, as yet, acquired official cognizance.

Oxophenarsine hydrochloride ("Mapharside") and oxophenarsine tartrate ("Neo-Halarsine") are added to the organic arsenicals.

Dimercaprol (BAL) is presented without any indication as to its dosage, and no mention is made of any official injection—surely an oversight in view of the varying strengths and vehicles of the proprietary forms.

Methacholine chloride is added to the growing list of cholinergic drugs and isoprenaline sulphate to the adrenergics.

Cetrimide ("Cetavlon")—one of the quaternary ammonium compounds structurally related to methacholine—represents the cationic group of detergents and antiseptics of which, perhaps, the better known are the benzalkonium chlorides of the "Zephiran" type.

Dicophane (DDT) is the sole representative of that large group of insecticides and repellents now assuming a place of increasing importance in preventive medicine.

The introduction of tubocurarine chloride, described as the salt of an alkaloid obtained from plants of the genus *Chondrodendron*, is an interesting reminder of other days. In the British Pharmacopœia 1898 a root from a plant of this genus was official for the production of a liquid extract which found much favour when administered orally for the treatment of chronic inflammation of the genito-urinary tract.

Other monographs devoted to new drugs describe ethinylœstradiol, propylthiouracil and the diagnostic reagents indicarmine, pheniodol and phenolsulphonphthalein.

The appendices follow the usual pharmacopœial pattern. Of interest among the additions are details relating to the biological assays of streptomycin and tubocurarine and the determination of A B O groups and Rh groups in human blood.

With so much therapeutic material available, the task of discrimination becomes increasingly difficult and the publication of an Addendum represents but one phase in a continuous process of research and selection.

The British Pharmacopœia Commission once more earns appreciative thanks for a good job well done.

Notes on Books, Current Journals and New Appliances.

ABBREVIATIONS IN SIX LANGUAGES.

UNDER the title *"Pars pro toto"* and the subtitle *"Breviarium medicum internationale"* (in the only language yet to attain real international status), Alfred Peyser has assembled a handbook of abbreviations and their meanings from the literature of medical and allied sciences in six languages—English, German, French, Italian, Spanish and Swedish.[1] A wide range is covered. The aim has been to present abbreviations used in medicine as completely as possible with a representative collection from allied sciences and important other abbreviations met with by the medical reader. Information is given both about the etymology of the abbreviated terms and on their application, where the author thinks this is expedient. It is to be regretted that the distinction between Australian and Australasian is apparently not appreciated on the other side of the world; a much too common error is perpetrated by the interpretation of F.R.A.C.P.(S.) as Fellow of the Royal Australian College of Physicians (Surgeons). A curious omission is F.R.S. However, in a world where abbreviations, official, unofficial and fantastic, abound, this attractively produced little book should receive a warm welcome. Inclusion of an abbreviation in this book does not, it is presumed, imply approval of it by the author of the book or by anyone else except its own originator; but the author, by not allowing himself to be shocked by literary bad taste or obscurity of expression, has produced a catholic list of considerable interpretative value.

[1] *"Pars Pro Toto: Breviarium Medicum Internationale"*, by Alfred Peyser; 1950. Stockholm: Almqvist and Wiksell. 6½" × 4½", pp. 196. **Price: 21s.**

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Modern Treatment Year Book, 1951: A Year Book of Diagnosis and Treatment for the General Practitioner", edited by Sir Cecil Wakeley, K.B.E., C.B., M.Ch., D.Sc., P.R.C.S., F.R.S.E., F.A.C.S., F.R.A.C.S. (Honorary); 1951. London: Published for The Medical Press by Baillière, Tindall and Cox. 9" × 6", pp. 382, with 61 illustrations. Price: 17s. 6d.

Issued by The Medical Press, the book contains 39 articles on a variety of subjects.

"Human Physiology", by Bernardo A. Houssay, M.D., Juan T. Lewis, M.D., Oscar Orías, M.D., Eduardo Braun Menendez, M.D., Enrique Hug, M.D., Virgilio G. Foglia, M.D., Luis F. Leloir, M.D., translated by Juan T. Lewis, M.D., and Olive T. Lewis, with a foreword by Herbert M. Evans, M.D.; First Edition; 1951. New York: McGraw-Hill Book Company, Incorporated. 10" × 7½", pp. 1134, with 499 illustrations. Price: $14.00.

Written for "students who have no knowledge of pathology, but who must acquire the physiological basis necessary for the study of disease and the practice of medicine".

"Royal Northern Operative Surgery", by the surgical staff of the Royal Northern Hospital; Second Edition; 1951. London: H. K. Lewis and Company, Limited. 10" × 7", pp. 646, with 498 illustrations. Price: 90s.

The book "represents the practice and teaching of men who have had a wide experience of different branches of surgery".

"Bacterial and Virus Diseases: Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment", by H. J. Parish, M.D., F.R.C.P.E., D.P.H.; Second Edition; 1951. Edinburgh: E. and S. Livingstone, Limited. 7½" × 5", pp. 212, with about 20 illustrations. Price: 10s. 6d.

Deals with essential principles and their practical application.

"Atlas of Tumor Pathology: Tumors of the Adrenal", by Howard T. Karsner, M.D.; 1950. Washington: Armed Forces Institute of Pathology. 10½" × 8", pp. 60, with 47 illustrations. Price: $1.00.

Deals with tumour-like lesions, cortical and medullary tumours, melanomata and secondary tumours.

"Medical Botany: A Hand-book for Medical Men and all who are Concerned in the Use of Plants: Nutritionists, Dieticians, Pharmacists and Veterinarians", by Alexander Nelson, Ph.D., D.Sc., F.R.S.E.; 1951. Edinburgh: E. and S. Livingstone, Limited. 8½" × 6", pp. 556, with 16 plates and 13 text figures. Price: 30s.

Claimed to present "all the evidence required for a discussion of the many problems in human welfare where plants are concerned".

"The Organization of Bones", by P. Lacroix, translated from the amended French edition by Stewart Gilder, B.Sc., M.B.; 1951. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 244, with 87 illustrations. Price: 25s.

The subject is studied chiefly by the microscope and by radiological methods.

"The 1950 Year Book of Endocrinology (January, 1950-January, 1951)", edited by Willard O. Thompson, M.D.; 1951. Chicago: The Year Book Publishers, Incorporated. 8" × 5½", pp. 500, with 138 illustrations. Price: $5.00.

One of the "Practical Medicine Series" of Year Books.

"Annual Review of Medicine", edited by Windsor C. Cutting and Henry W. Newman; Volume II; 1951. Stanford, California: Annual Reviews, Incorporated. 9" × 6", pp. 494, with a few illustrations. Price: $6.00.

Contains nineteen articles by different authors on selected subjects in internal medicine.

The Medical Journal of Australia

SATURDAY, AUGUST 18, 1951.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

SJÖGREN'S SYNDROME.

THE interest among Australian practitioners in Sjögren's syndrome is due largely to the contributions on the subject that have been made from time to time by J. Bruce Hamilton, of Hobart, and to his translation of Henrik Sjögren's monograph, "A New Conception of Keratoconjunctivitis Sicca", published in 1943. In this monograph Sjögren reviews the literature and describes the ocular disease as being of slow commencement, having a chronic course with remissions and occurring mostly in women of mature years. The subjective symptoms are: itching, burning, a sensation of the presence of a foreign body, photophobia, a feeling of dryness with an inability to weep and diminution of visual acuity. The objective ocular signs are: hyperæmia of the conjunctiva with papillary hypertrophy, thready conjunctival secretion, slight ciliary injection, unevenness of the cornea with grey patches in the epithelium or minute superficial corneal infiltrates, firmly adherent corneal epithelial filaments, at times slight diminution of the corneal sensibility and diminished lachrymal secretion. Ocular complications are never found. Among "other noteworthy, although not constantly present, symptoms" Sjögren noted diminution of the salivary secretion, periodical parotid swelling (occasionally combined with fever), atrophy of the lingual and oral mucous membrane, falling out of the teeth, arrest of the sweat secretion and arthritic changes.

Phillip Ellman, F. Parkes Weber and T. E. W. Goodier, who publish an article entitled "A Contribution to the Pathology of Sjögren's Disease",[1] refer to a report by R. B. Raffle which appeared in the *British Medical Journal* of June 24, 1950. Raffle's case shows that the eye lesion may not be the presenting feature, but that patients may first seek advice because of enlargement of salivary glands or because of xerostomia. Raffle's patient, a woman, was found to suffer from a severe vitamin deficiency. Under treatment the general condition became less abnormal, but the dryness of the oral mucosa and so on which were thought to have allowed the vitamin deficiency to have occurred, remained unchanged. This patient may later, it would appear, suffer from eye changes. Ellman, Weber and Goodier point out that in its complete form Sjögren's disease includes *keroconjunctivitis sicca*, xerostomia, *keratitis sicca*, *pharyngitis sicca*, and *laryngitis sicca*; they add that incomplete forms are more often seen. They point out that the chronic inflammatory changes in the parotid glands tend to produce permanent enlargement, or sclerosis, or atrophy, in irregular combination. Analogous changes occur in the other salivary glands, in the oral mucosal glands, and also, though as a rule without obvious clinical enlargement, in the lachrymal glands. No doubt, as our authors suggest, many cases of Sjögren's disease have been labelled Mikulicz's disease, and according to old nomenclature all cases of Sjögren's disease in which there is any clinical enlargement of salivary glands, even without definite enlargement of the lachrymal glands, might be classed as cases of Mikulicz's syndrome due to unknown pathogenic agents. The sweat glands of the skin and the acid-producing glands of the stomach may be involved.

In the case described by Ellman and his co-workers the dryness of the bronchial mucosa played the most disastrous part. The patient was a woman, aged thirty-four years, and her clinical history is given in detail. The post-mortem findings are minutely described and a special report on sections is given by Professor Dorothy S. Russell. It is interesting to note that when she was twenty-one years of age, the patient, after suffering from scarlet fever, had bilateral swelling of the face which was thought to be due to mumps. In January, 1942, painless parotid swellings were thought to be due to Mikulicz's disease. In 1948 she complained of dryness of eyes, mouth and throat and of an irritable cough which was worse when she talked. She had to take frequent sips of water when she talked. Sometimes she had difficulty in swallowing. At the end of March, 1949, she had a spontaneous pneumothorax on the right side. The pleura of the left lung was involved. She died in June, 1949, of acute pulmonary œdema due to left-sided failure of the heart. Signs of acute bronchopneumonia were found *post mortem*. It is to be noted that with fluorescein both corneæ showed punctate staining; filamentary epithelial shreds were present in the left eye and almost total xerophthalmia and a corneal ulcer were present in the right eye.

Professor Russell describes the appearances seen in stained sections. She writes that the significant histological changes are remarkably uniform and affect the left and right lachrymal glands, the parotid gland (only one was examined) and the submaxillary glands. In addition she draws attention to the following mucosæ and their subjacent secretory glands: conjunctival, buccal, lingual, nasal and naso-pharyngeal, faucial, epiglottic, laryngeal, tracheal, bronchial and œsophageal. Related changes were present in the skin. The glands were the site of degeneration and atrophy and the mucosæ were affected by chronic inflammation. There was no evidence of the nature of the agent responsible for the inflammation. The pulmonary changes which were extensive were interpreted by Professor Russell as a secondary development promoted by the absence of normal secretions from the tracheal and bronchial mucosæ. In the middle lobe of the right lung the appearances were suggestive of lipoid pneumonia and this was explained as possibly due to oily medicaments used by the patient to lubricate the upper respiratory passages. The changes in the mucosæ

[1] *The Quarterly Journal of Medicine*, January, 1951.

are summarized as consisting of diffuse infiltration of the *lamina propria* with small lymphocytes, plasma cells and occasional neutrophile leucocytes. Professor Russell thinks that probably the chronic inflammatory infiltration of the *lamina propria* of the mucosæ is a secondary manifestation.

The conclusion of the study is that the pathological basis of the dryness of the mucous membranes and skin consists in a chronic inflammatory atrophy of unknown causation involving the salivary, lachrymal, mucosal and sweat glands. This is admittedly inconclusive, but it is all that emerges from what the authors describe as the most complete histological study of a case of Sjögren's disease. One or two remaining considerations may be mentioned. The question is asked why the affected lachrymal glands in Sjögren's disease never appear to be clinically enlarged, although such enlargement has occurred in cases regarded as Mikulicz's disease or Mikulicz's syndrome. It is also remarkable that ozœna, though apt, especially in women, to accompany atrophic rhinitis, seems to be absent in Sjögren's disease. The final point to be noted is that in the case described by Ellman, Weber and Goodier the thyreoid, pineal and pituitary glands were normal.

Current Comment.

LOW FREQUENCY VIBRATIONS OVER THE PRECORDIUM.

MEASUREMENT is one of the ideals of applied scientific method today, and rightly so, provided that we recognize not only the errors inseparable from measurement, but also the fallacies in figures. In the examination of the heart the classic methods of inspection and palpation are as valuable as ever if allied to careful observation and sound judgement, and auscultation supplies information about phenomena made manifest through hearing. These methods enable the observer to assess the significance of vibrations which can be appreciated by touch, sight and hearing. To these we add hydrostatic methods, aided once more by touch, sight and hearing, and enlist electrical and other technical devices to record the action story as told by the heart and its component structures. With perhaps a touch of cynicism we may then say that all that remains is to integrate all this information and build on this and other data diagnosis and prognosis. It is helpful and stimulating to find that those vibrations of low frequency which we can examine by the unaided senses can be measured, and that their importance can thus be demonstrated, even though no clinician ever needs to be reminded that pulsations in the veins of the neck or palpable thrills in the precordium are highly important. Franklin D. Johnston and Donald C. Overy have recently published an account of a simple technique whereby the precordial vibrations with a frequency below that of audibility can be recorded.[1] Using the modern optical methods in place of the old rather clumsy tambours and smoked paper, several investigators have achieved precision and simplicity, and, although some of these workers have thought that little was likely to emerge from further studies, the present authors consider that this little explored field is worth more attention. They have used a commercially produced electromanometer with an oscillating circuit and a balanced bridge with a device which allows pressure variations to be accurately measured. In this instrument a closely fitting chest-piece transmits vibrations from the precordium by air conduction with very little time lag; this is not significant in vibrations below the acoustic level. Special arrangements were necessary to prevent air leaks at the chest-piece, a trouble which will be recalled by any who have in the past played with any of the old types of polygraph, when these were used by patient clinicians trying to be scientists. Vibrations of two kinds were recorded—those due to displacements of the precordium, that is, displacement curves, and those due to waves proportional to the velocity of the movements of the chest wall. The latter were more closely related to the functional status of the myocardium, and therefore thought to be of greater clinical significance. The authors present a number of tracings, shown with coincidental electrocardiograms. Most of the records were made from vibrations registered at the position of the apex beat. These records are discussed in terms of the clinical examination and the general cardio-vascular state of the patient as already known from other investigation. Some of the conditions so studied were associated with definite or severe structural change, such as constrictive pericarditis, or valvular heart disease. Others were less definitely associated with gross anatomical changes, such as hypertensive states, with and without nephritis. It is evident that such work as this can be followed only by a personal study of the clinical state and the actual recordings. The authors sum up their work by pointing out that the set-up is not complicated, but yet has the advantage of recording static pressures by making accurate tracings of low frequency vibrations due to precordial displacements and, with the addition of a differentiating circuit, velocity curves of these movements. The crux of the work may for some lie in the last few lines of the article, which state that the clinical importance of these curves is related to the fact that they are quite inaudible, and yet are often visible or palpable. This is in line with numbers of other investigations of cardiac conditions which produce physical signs readily elicited at the bedside, whose inner meaning has been made clearer by an appeal to instrumental methods. Perhaps the real value in such observations lies in the encouragement they give to the prosecution of rapid skilled examination, which will become more trustworthy in proportion as it is checked by living physiology and pathology.

[1] *Circulation*, April, 1951.

VENTRICULAR FIBRILLATION DURING ANÆSTHESIA.

CHLOROFORM, although used seldom now as an anæsthetic agent, has yielded a great deal of experimental information about the anæsthetic state and its hazards. The peculiar danger of the combination of chloroform and adrenaline is well known, and the susceptibility of various animals to the production of ventricular fibrillation while under chloroform anæsthesia has been explored in the laboratory. The subject is still one of interest, especially as the occurrence of cardiac irregularities during the administration of cyclopropane is a well-known phenomenon in the use of this valuable anæsthetic. D. E. Hutcheon has recently remarked that very few comparative studies have been made in which anæsthesia with chloroform and cyclopropane has been induced to various stages in animals of different species. This worker has carried out studies of this nature, and observed the effect of the injection of adrenaline at these different stages.[1]

Control of changes in depth of anæsthesia was simply gained by bubbling air through chloroform into a cylinder covering the animal's head, and by administering cyclopropane from a spirometer, the carbon being removed from the system by soda lime. The depth of anæsthesia was judged by the presence or absence of the corneal reflex, the rate and depth of the respiration and the degree of muscular relaxation. The heart was observed by a stethoscope or by an electrocardiograph, and in addition direct examination of the heart was made in some instances. The animals observed included dogs, cats, rabbits, guinea-pigs and rats. The smaller species were immediately subjected to autopsy if the respirations ceased and the heart sounds

[1] *British Journal of Pharmacology and Chemotherapy*, March, 1951.

were no longer audible, and the state of the heart and lungs was examined. Ventricular fibrillation could be visually demonstrated in some of these animals by the rapid tremulous contractions of small areas of the muscle of the ventricles. Certain differences were observed in the effect of chloroform and cyclopropane in the different types of animal. In guinea-pigs the intramuscular injection of adrenaline during light chloroform anæsthesia caused fibrillation, but light cyclopropane anæsthesia had no such effect. Deep anæsthesia pressed beyond the danger point caused death from respiratory failure. Rats and rabbits, on the other hand, showed no signs of ventricular fibrillation after the injection of adrenaline during light or deep anæsthesia with chloroform or cyclopropane. In cats ventricular tachycardia could be caused, but not fibrillation, during either chloroform or cyclopropane administration. One exception to this summary should be noted; one cat died from ventricular fibrillation during the induction period of cyclopropane. In dogs, adrenaline injected intravenously during light chloroform anæsthesia always produced ventricular, or in one instance auricular, tachycardia, which in half the cases merged quickly into fatal fibrillation. Cyclopropane, however, did not predispose the animals to cardiac disturbances from adrenaline other than ventricular extrasystoles or transient tachycardia, provided the anæsthesia was of light depth. But if the cyclopropane was administered in dosage which produced slow shallow respirations death was easily caused from fibrillation of the ventricles. A further observation was made on dogs to see if the administration of "Dibenamine" would provide an antagonist to adrenaline, so that the risk of the otherwise fatal combination of chloroform and adrenaline would be averted, but no effect was observed which could with certainty be interpreted in this way. Fibrillation followed in two animals out of eight, and all the others had transient tachycardia. Further observations might be worth while on this point.

This series of experiments once again illustrates the difference in the reactions of animals of different species to the same drugs, but it also shows differences in susceptibility within the same species. The moral with the human species is clear. Fortunately the specialty of anæsthesia rests on a firm foundation which expands year by year as additions to mechanical and pharmacological knowledge are made. Hutcheon's work introduces no novel ideas, but it helps to consolidate that foundation.

THE NITROGEN MUSTARDS.

ATTENTION has been drawn during the last few years to the possibilities of the nitrogen mustard compounds in the treatment of neoplastic disease. Although only five years have elapsed since the palliative effects of these drugs were first seriously studied, a great deal of work has been done on the subject. There are grave drawbacks to the use of any of the substances which arrest neoplastic processes such as leuchæmias, lymphomata and the Hodgkin group, the chief being the severe toxic effects on the bone marrow. Nitrogen mustard has given much trouble also with its tendency to cause damage to veins and still more to subcutaneous tissues if it escapes from a vein, and its proneness to set up gastric irritation has made it unpopular with patients. However, experiments made during the war which were carried out in order to ascertain the hazard in drinking water contaminated with nitrogen mustard showed that leucopenia was produced when the substance was administered orally. This gave reason to hope that if the toxic fractions could be eliminated or modified the drug might be used by the oral route. So far, however, the hope of separating the molecular fractions or groups responsible for the different therapeutic and toxic properties has not been realized until recently, when the introduction of other molecular variants of the nitrogen mustards seems to loom over the horizon. The combined efforts of several scientific bodies in New York and a team of investigators (D. A. Karnofsky, J. H. Burstenal, G. C. Armistead, C. M. Southam, J. L. Bernstein, L. F. Craver and C. P. Rhoads) have produced some interesting results by comparing the effects of triethylene melamine administered to patients suffering from several varieties of neoplastic disease.[1] They point out that hitherto toxic effects of methyl-*bis*-(2-chloroethyl) amine, the substance usually administered, have not been found separable from the desired action on the bone marrow, but the discovery of the tumour-inhibiting power of triethylene melamine, allied to its much lower capacity to cause nausea and vomiting, has raised hopes again. There is a good deal of experimental evidence in favour of this substance, and study of its structural formula suggests that chemists may produce other and perhaps more useful drugs of this series. Laboratory studies show that the compound is readily soluble in water, though small amounts of an insoluble polymer may also be present. The toxic effect on dogs is only half as great when it is given by mouth, though the general nature of the tissue changes seen after lethal doses is the same as in the methyl-*bis* type of the drug. A feature of difference which attracted the attention of the investigators was the absence of any convulsive or cholinergic effect. It should be noted, however, that in animal tests it could not be foretold which type of toxic effect would predominate, the gastro-intestinal or the hæmatopoietic. Clinical studies were carried out on two series of patients, one receiving the drug by the oral route and the other by the intravenous. During the first year of the investigation, which began in 1949, 58 persons were given the drug by the oral route, and 36 were treated by intravenous injections. The latter series included patients suffering from various types of leuchæmia, Hodgkin's disease, lymphosarcoma, carcinoma of the lung, and advanced neuroblastoma. The oral series covered much the same variety of neoplastic disease, but is being extended somewhat in more recent work, now that the technique and the precautionary measures are better understood. The hæmatological effects of the drug were estimated in five categories, graded for the purpose of comparison. Considerable variation was found in the individual tolerance of those receiving intravenous treatment; naturally the clinical state of the patients had to be taken into account. As the effect of the drug is cumulative, and a latent period intervenes before the full effect on the sensitive bone marrow is observed, spacing of doses needs the greatest care. The toxic effects of the drug when given orally were the same in type as when it was given intravenously. The problem, of course, was to deliver an effective therapeutic dose without exciting dangerous reactions. The dose was simply given in tablet form, and immediate reactions were very rare. Side effects appeared sometimes after some hours, but the most important toxic signs and symptoms were delayed. One point of interest may be mentioned: it has been found that severe gastro-intestinal disturbance after high dosage has been often accompanied by loss of taste or persistent bad taste. Without forcing speculation too far it may be recalled that this symptom is sometimes seen in Addison's disease.

It is impossible here to deal with the authors' experiences and findings; only a few can be summarized. The authors have found in triethylene melamine a substance with properties similar to the previously used nitrogen mustards; its value is enhanced by its toleration when given by mouth. A dose of 20 to 40 milligrammes may usually be given in a three to five week period. Its use has been followed by temporary improvement in Hodgkin's disease, lymphosarcoma, chronic leuchæmias of lymphocytic and myelogenous types, and *mycosis fungoides*. The results with miscellaneous varieties of neoplasms have been unsatisfactory, but the authors feel that investigation should be continued. Triethylene melamine is a very dangerous drug, like its congeners, and overdosage will inevitably produce severe depression of the function of the bone marrow. Finally it must be understood that the place of this drug in clinical practice depends upon its capacity to act like other similar agents, such as irradiation, urethane, and radio-active phosphorus, and that its use does not deter the clinician from using these other methods in addition during the course of the disease.

[1] *Archives of Internal Medicine*, April, 1951.

Abstracts from Medical Literature.

BACTERIOLOGY AND IMMUNOLOGY.

Coproantibodies in Dysentery.

L. M. GONZALEZ, G. ARBONA AND J. FERNOS (*The Journal of Infectious Diseases*, September-October, 1950) began studies in bacillary dysentery by describing failure to detect coproantibodies in patients with bacillary dysentery (Flexner). The infecting organism, which is confined to the bowel and to the local area of infection, is known to be associated with a low titre of serum antibodies. Detection of coproantibodies in experimental infection of the guinea-pig by the cholera organism has been recorded. This study was made on fæcal material from dysenteric patients in a psychiatric hospital ward. Blood samples were also taken. Cultures were made from fæces, which were then allowed to undergo extraction in formol saline overnight; the supernatant fluid was purified by centrifugation, and tested for the presence of agglutinins against the cultures from the same patient which had been identified in the routine way. Serum titres were also tested on these cultures. The serum contained antibodies detectable in dilutions of the patients' serum from 1:40 to 1:1280. The results of tests on extracts of fæcal suspensions were always negative. The serum antibodies tended to increase during the patient's illness.

Combinations of Antibiotics and Enterococci.

JANET B. GUNNISON, E. JAWETZ AND VIRGINIA R. COLEMAN (*The Journal of Laboratory and Clinical Medicine*, December, 1950) have studied the effect of combinations of antibiotics on enterococci *in vitro*. The test organisms were strains isolated from five patients with subacute bacterial endocarditis and from twelve patients with urinary tract infections. Large inocula of 10^8 to 10^9 organisms from cultures eighteen to twenty hours old were used in order to increase the likelihood of resistant forms, and cultures were observed and tested for up to twenty-eight days. The test materials contained varying amounts of penicillin combined with a single concentration of the second substance; an estimate was made of the number of colonies growing in subculture. The minimal initial concentration preventing visible growth for four days was called the "static" concentration. The lethal concentration was that killing 99·9% of organisms in twenty-eight days, while penicillin also had an "optimal" concentration—that which produced the most rapid death rate in forty-eight hours, without killing all the organisms; this amount usually lay between 6 and 30 units of penicillin per millilitre. Streptomycin had no effect in amounts less than 250 milligrammes per millilitre. A combination of penicillin and streptomycin showed enhanced effect, reducing the amount of both drugs needed for bacteriostasis and bactericidal effect; and viable organisms less often persisted after activation of the penicillin. These "persisters" were tested for sensitivity to the individual drugs, but no variations could be demonstrated. Penicillin and aureomycin were antagonistic in their effects on enterococci, while the addition of chloramphenicol, though it increased the ultimate bactericidal action of penicillin, reduced its rate. Mixtures of three and four antibiotics were also studied, and the presence of chloramphenicol always seemed to decrease the killing power of the mixture. The authors discuss the significance of their findings in these relatively resistant organisms, and the clinical wisdom of combinations of antibiotics in treatment. They point out that limited knowledge of the mechanism of their action, together with the demonstration *in vitro* of antagonistic action between them, should indicate caution in such procedures, with the possible exception of a combination of penicillin and streptomycin.

Production of Cytoplasmic Bodies by Lymphocytes.

R. WILLIAMSON (*The Journal of Pathology and Bacteriology*, January, 1950) has studied the production of cytoplasmic bodies by lymphocytes. Using lymph nodes from normal rabbits, he made impression preparations rapidly after the death of the animal, fixed them in Helby's fluid and used various staining methods. He states that the pseudopodia of lymphocytes so rarely seen in films from peripheral blood were frequently visible, and small cytoplasmic bodies, in which mitochondria were present, could be demonstrated. He discusses the possibility that this is the mechanism by which large lymphocytes become small, and that it may be a means by which the γ globulin is distributed throughout the body.

Preparation of Specific Polysaccharides of Pneumococcus.

M. HEIDELBERGER, C. M. MACLEOD, H. MARKOWITZ AND AMY S. ROE (*The Journal of Experimental Medicine*, April, 1950) have studied and improved methods for the preparation of the specific polysaccharides of the pneumococcus. They emphasize the fact that contact with alkali invariably decreases the yield of polysaccharide from a culture, and exemplify this by measuring the amount of precipitate obtained with the homologous antiserum prepared in rabbits. They have shown that in 0·1 N sodium hydroxide solution, the polysaccharide will fall to only 7% of its original strength if left for six days at room temperature. Careful directions are given for methods giving maximal yields in several pneumococcal types.

Non-Hæmolytic Streptococci from the Respiratory Tract.

FRANK L. HORSFALL, JUNIOR (*The Journal of Experimental Medicine*, March, 1951), began studies on non-hæmolytic streptococci isolated from the respiratory tract of man with an assessment of the antigenic basis for type-specific reactions with *Streptococcus salivarius* and non-levan-forming streptococci. In the authors' laboratory, previous work had established the type specificity of the capsular polysaccharide of *Streptococcus salivarius* and its similarity to that found in the strain known as "M.G.". It was also shown that in the presence of sucrose, the organism could synthesize levan. Two distinct serological types can be identified by each of these methods, the polysaccharide of each being part of the bacterial surface, the other being demonstrable only when the organisms have been grown in the presence of the substrate sucrose. The levans formed by the two strains appeared to be identical.

Propagation of Dengue Virus.

R. W. SCHLESINGER (*The American Journal of Hygiene*, March, 1950) has observed the propagation in chick embryos of the Hawaiian strain of dengue virus. He records sustained serial passages in eggs after 101 intracerebral passages in mice; this had not been achieved before the strain had become mouse-adapted. After 38 passages through eggs, opportunity was taken to inoculate egg material into two human patients suffering from nephrosis. This was done because such patients have been known to exhibit striking improvement after an attack of virus disease such as measles. The inoculations were made subcutaneously. One patient had no clinical signs, but the other had a rash and fever on the ninth and tenth days after inoculation. Attempts to isolate virus from the patients failed, but the serum of both developed protective antibodies against infective virus in eggs. No complement-fixing antibodies could be demonstrated.

Inhibition of Diphtheria Bacillus by Saliva.

R. THOMPSON AND ANN JOHNSON (*The Journal of Infectious Diseases*, January-February, 1951) have studied hydrogen peroxide, the inhibitory agent produced by salivary streptococci, in the inhibitory action of saliva on the diphtheria bacillus. They used pour plates of diphtheria bacilli, and then planted various strains of salivary streptococci upon them. Circles of inhibition of growth were seen, and if a staphylococcus was inoculated near by, a segment of the circle of inhibition was eliminated. It was shown that the great majority of organisms which inhibited the growth of diphtheria produced hydrogen peroxide, and it was further shown that the organisms which could interfere with this effect were organisms which produced catalase. Strains of bacteria were compared in their susceptibility to inhibition by saliva, by salivary streptococci and by hydrogen peroxide; the order of sensitivity was the same to all three agents.

HYGIENE.

Occupational Dermatitis in the Citrus Fruit Canning Industry.

D. J. BIRMINGHAM, P. C. CAMPBELL, H. N. DOYLE AND J. M. MCDONALD (*A.M.A. Archives of Industrial Hygiene and Occupational Medicine*, January, 1951) have conducted a survey of 1200 workers employed in the Florida citrus fruit canning industry to determine the incidence, the causes and the means of preventing occupational skin diseases in that industry. The occupational skin diseases noted consisted mainly of contact dermatitis, onychia, paronychia, burns and callosities of the palm, *erosio interdigitalis blastomycetica* and knife-blade lacerations. Patch tests were carried out with grapefruit and orange pulp and juice on volunteers who were affected with dermatitis. It is stated that in the majority of cases "citrus dermatitis" does not occur on the basis of specific sensitization. The workers did not

react to the pulp and juices of fresh grapefruit and orange. However, one employee reacted to alkali-treated grapefruit pulp and another to alkali-treated orange pulp. These two reactions may mean that insufficient washing of the fruit after the alkali bath permits residuum of alkali, which irritates the skin of some workers who are highly sensitive to alkali. Patch tests carried out with broken peel of grapefruit and orange on five volunteers verified that all persons show pronounced skin reaction to citrus peel oil, which is a primary irritant. Operators of juicing machines had little or no dermatitis, because the mechanical juicing machines minimize the contact with citrus juices and oils. The authors made the following recommendations to prevent occupation dermatitis in the industry concerned: Cotton-lined rubber gloves and impervious sleeves should be worn by those peeling and cutting the fruit into sections. Washable leather or fabric gloves should be worn by those handling the whole fruit. Impervious aprons should be worn by all employees. Adequate washing facilities with mild toilet soaps or sulphonated oil detergents should be provided. Refatting agents like lanolin should be used on the hands after washing. Medical records should be kept. Mechanical enclosed methods of canning should be used whenever possible.

The Treatment of Lead Poisoning with Sodium Citrate.

H. HARDY, R. BISHOP AND C. MALOOF (*Archives of Industrial Hygiene and Occupational Medicine*, March, 1951) report results obtained by the use of sodium citrate in the treatment of lead poisoning. The history, signs and symptoms, and results of investigation in each case are given. The relationship between the amount of lead and coproporphyrin in the urine was investigated, and in all four cases the values of these two substances showed relatively good correlation. In acute cases coproporphyrinuria was always present much earlier than stippled red cells. The cause of coproporphyrinuria in lead poisoning is discussed. The authors conclude that oral administration of sodium citrate will control the symptom of lead poisoning, but that studies of lead excreted in the urine in these four cases did not warrant the conclusion that sodium citrate increases lead excretion.

Tuberculosis in Mental Hospitals.

JOSEPH D. WASSERSUG AND WILLIAM F. MCLAUGHLIN (*The Journal of Nervous and Mental Disease*, February, 1951) discuss the incidence of tuberculosis in mental hospitals. They state that in New York State in 1940-1941 photofluorography revealed that 4·7% of 68,743 patients had clinically significant tuberculosis. In Oklahoma the occurrence of tuberculosis in mental hospitals is ten times more frequent than among the general population. Such findings are not confined to these States, and they are reflected in the tuberculosis rate among mental hospital employees. Of 14,228 employees in New York mental hospitals no less than 1·1% had clinically significant tuberculosis. The incidence is approximately twice as high as that among industrial workers. The authors plead for the wide recognition of the problem and insist on the use of thorough methods of recognition and treatment. They state that all new patients and all new employees must be examined radiologically. Surveys should be repeated at stated intervals or be an annual affair. The authors stress the fact that the X-ray examination does not detect every tuberculous lesion. Examination of the sputum for tubercle bacilli is most important. The sedimentation rate determinations and the tuberculin test are also helpful. Sputum is often difficult to obtain from patients. Gastric or bronchial lavage often yields positive results. It is noted that pneumothorax may be curative of mental symptoms in some cases. Also that pneumothorax does not contraindicate electroshock.

The Incidence of Subclinical Poliomyelitis.

A. CASEY, W. FISHBEIN, F. SCHABEL AND H. SMITH (*American Journal of Public Health and The Nation's Health*, October, 1951) have attempted to determine the incidence of poliomyelitis infection in an urban area by direct virus isolations. Stools were collected in Chicago during 1945 and 1946, from 260 "contact", "non-contact" and "control" children. From the stools a total of 576 monkeys were inoculated. Virus was recovered from the stools of 54 of 101 "contact", six of 55 "non-contact", and eight of 104 "control" children. Twelve of the 14 "non-contact" and "control" children with positive findings were one to four years of age. Eight of 10 familial "contacts" and 38 of 49 non-familial "contacts", one to five years of age, yielded positive findings; six of eight familial "contacts" and seven among 30 non-familial "contacts", six years of age and older, yielded positive findings. It was calculated that most children in Chicago had probably had poliomyelitis once by the fourth birthday, and 75% perhaps twice by the sixth birthday, either from different strains or from reinfection. The authors state that from these calculations it would appear that on the average over 100,000 to 125,000 cases of poliomyelitis occur in Chicago each year, affecting 3% to 4% of the total population. There is a similarity in the estimates of poliomyelitis infection in urban populations in relation to age, whether determined by virus isolation, by sparing after virus challenge, or by neutralizing antibody response.

Evaluation of the Astoria Plan of School Medical Services.

A. YANKAUER (*American Journal of Public Health and The Nation's Health*, April, 1951) has carried out an investigation to determine the case-finding effectiveness of an elementary school medical service designed on the Astoria Plan. The essential features of the Astoria Plan is an annual "conference" on the health of each school child by the teacher and the school's nurse. The school medical officer examines all children when they commence school, when they reach eighth grade standard and when they are referred by the teacher or nurse. In the author's investigation 334 elementary school children, representing 1560 student years in the New York City school system, were examined. The examination, in addition to a routine medical examination, included hæmoglobin determination, urine examination for sugar and albumin, Snellen chart testing, evaluation of hearing with a pitch tone audiometer, tuberculin patch testing and nutritional analysis of a one-day food intake. There were 247 adverse conditions observed in 182 children (55% of the total examined). The three most common adverse conditions were visual (33% of all children examined), nutritional (12·5%), and behaviour and emotional conditions (10·7%). The most common nutrient deficiency was that of ascorbic acid. Of these adverse conditions only 22 were not previously known to the school medical service, and these were of a mild nature. The author concludes that the Astoria Plan of school medical service functioned satisfactorily as a case-finding mechanism and provided for the efficient utilization of professional services within the school.

Diarrhœa, Dysentery, Food Poisoning and Gastro-Enteritis.

M. FEIG (*American Journal of Public Health and The Nation's Health*, November, 1950) gives an account of a study of 926 outbreaks that included 49,879 cases of diarrhœa, dysentery, food poisoning and gastro-enteritis reported to the United States Public Health Service for the years 1945-1947. He considers that a great deal of the confusion existing today in our understanding of the commoner forms of gastro-enteritis is basically due to poor diagnostic terminology, in which unrelated syndromes are often classified independently. He suggests that the present trend toward ætiological diagnosis, employed to some extent by bacteriologists and health agencies, be utilized by the clinician, and that the laboratories be used to a greater extent as a diagnostic tool. He also stresses the need for additional clinical data in the differentiation of the various forms of acute gastro-enteritis. He states that of the 926 outbreaks of gastro-intestinal disease, the causative organism was determined in 478. Staphylococci were implicated in 78%, salmonellæ in 15%, streptococci in 7% and shigellæ in 3% of the outbreaks. The mean incubation period for the staphylococcal group was 3·9 hours, for the salmonella group 18·2 hours, for the shigella group 53·4 hours and for the streptococcal group 10·3 hours. There were 378 food items involved in 304 staphylococcal outbreaks. Of these foods, 35% were meat products, 35% bakery products, 22% poultry, 8·6% potato products and 8·6% milk or milk products. Ham was the food involved in half of the outbreaks due to meat products, and cream or custard pastry was the food involved in 86% of the outbreaks due to bakery products. In the salmonella group meat and meat products were implicated in 28% of outbreaks, poultry in 18·5%, bakery products in 15%, milk and milk products in 15% and vegetables in 13%. Water was the food involved in two and milk in one of the thirteen outbreaks due to shigellæ. Of the eleven outbreaks caused by streptococci, poultry was the food implicated in four; meat products, bakery products and potatoes were each involved twice, and milk and milk products once. The case fatality rates available appeared to indicate that the age group affected was the determining factor rather than the infecting organism or toxin. The deaths recorded were in the early and late age groups.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held at the Children's Hospital, Carlton, Melbourne, on May 23, 1951.

Bronchiectasis following Primary Tuberculous Infection in Children.

DR. HOWARD WILLIAMS read a paper on bronchiectasis following primary tuberculous infection in children. He said that four years earlier he had examined a patient, P.F., aged four and a half years, in consultation with Dr. L. P. Wait. The patient had attended Dr. Wait's clinic in March, 1947, as she had been listless and off colour after a cold contracted six weeks previously; for it her family doctor had prescribed sulphonamide tablets. Examination of the child disclosed that she had impairment of the percussion note at the base of the right lung with diminished air entry and moist sounds audible at the end of inspiration. She was otherwise healthy. X-ray examination showed collapse of the lower and middle lobes of the right lung, bronchoscopy revealed no abnormality of the bronchial tree, and a bronchogram showed collapse and bronchiectasis of the lower and middle lobes of the right lung. Her Mantoux reaction with 1:1000 dilution of old tuberculin was positive, but culture of the fasting gastric contents for tubercle bacilli twice gave negative results. Her parents and relatives were free of tuberculous infection, and the child, so far as the parents knew, had not been in contact with any patient with tuberculosis.

Dr. Williams said that the patient presented an unusual picture for a child with collapse and bronchiectasis of two lobes of the right lung, as she had not suffered at any time with cough or sputum, had never been ill apart from the common ailments from which every child suffered, and had at no stage had any serious respiratory tract infection. Three questions could be asked on consideration of the child's illness. (i) What relation did the positive Mantoux test result bear to the lung lesion? (ii) What was the ætiology and mechanism by which the lobes became collapsed and bronchiectatic? (iii) What should be the treatment of the condition? Those were some of the problems that confronted him, Dr. Williams said, and the following account of a study of thirty patients with tuberculous infection of the lungs answered in part some of the questions.

A possible line of approach to the problems raised was suggested by the surprising bronchoscopic finding of watery-looking tuberculous granulation tissue, which was almost completely occluding the right main bronchus, in a young boy who was being investigated for collapse of the lower and middle lobes of the right lung. The patient, C.T., was a boy who at the age of four years developed a febrile illness and a cough and received sulphonamide treatment for one week from his family doctor for "pneumonia". He was not ill during that time and recovered rapidly, but was left with a dry residual cough. On clinical and radiological examination in August, 1948, he was a well-nourished active boy with collapse of the lower and middle lobes of the right lung, a positive Mantoux test result, and a growth of tubercle bacilli from the fasting gastric contents. The source from which the boy was infected could not be discovered; his parents and brother and sister were free from infection, but his maternal grandmother who had a chronic cough refused examination.

The boy clearly demonstrated one cause for collapse of a lobe in tuberculous infection, namely, ulceration of a caseous hilar gland into a bronchus, and it seemed reasonable and logical to seek out all available tuberculous patients with radioopacities of a lobar or segmental nature and investigate them clinically, bacteriologically and bronchoscopically, and to follow the natural course of the disease process. Thirty patients had been studied during the past three years; the result of the investigation, Dr. Williams said, had clarified considerably the ætiology and the mechanism by which primary tuberculous infection caused bronchiectasis.

Three case histories with radiographic illustrations were then shown, demonstrating the development of bronchiectasis from its earliest stages. The first patient illustrated collapse of the upper lobe of the left lung by occlusion of the left upper lobe bronchus by tuberculous glands. Gradually the collapsed lobe had retracted, leaving a residual bronchiectasis of the lingula segment. The second patient demonstrated collapse of the lower and middle lobes of the right lung from ulceration of a tuberculous gland into the right main bronchus. Gradually destruction of those two lobes occurred from a tuberculous inflammatory lesion in the collapsed segments. The third patient illustrated the development of a stricture of the right main bronchus from erosion of the bronchial wall by a tuberculous gland.

The first patient, M.P., who illustrated collapse of the upper lobe of the left lung from bronchial occlusion by tuberculous hilar glands, had reported to the hospital in November, 1947, at the age of one year, with the history that he had made excellent progress until nine months of age, when he contracted a cold, developed a cough and became rather fretful and failed to gain weight. Examination revealed clinical and radiological signs of consolidation of the upper lobe of the left lung, a strongly positive Mantoux reaction, but a negative result from culture of the gastric contents for tubercle bacilli on three separate occasions. During the next six months he improved, lost his cough and became very cheerful, but the clinical and radiological signs persisted in the upper lobe of the left lung, although on one occasion the apical segments cleared for a period of three months. Bronchoscopic examination in March, 1948, showed a blunted reddened *carina major*, with reddening and some narrowing of the left main bronchus, while the orifice of the upper lobe of the left lung was reduced to a mere slit. As he was gaining weight, entirely symptomless and very well, he was sent home in August, 1948, and observed as an out-patient. During the next year he was well, free of symptoms and gained weight; clinically his chest became normal, and radiologically the opacity slowly cleared, leaving a streaky appearance in the lingula and some calcification in the left paratracheal glands. Bronchoscopy at that time showed complete resolution of the previous changes, and a bronchogram showed cylindrical bronchiectasis with collapse of both pectoral and lingula segments. During the next twenty months the boy had had a number of the common respiratory tract infections, but all had cleared rapidly, and none had spread to the bronchiectatic portion of his left lung.

The second patient, D.D., illustrated the development of collapse and tuberculous suppuration following the ulceration of a tuberculous gland into the right main bronchus. In June, 1948, the patient, a baby, aged fifteen months, had developed "bronchitis" with wheezing breathing and malaise. As those symptoms persisted he was sent to the Children's Hospital for examination for a foreign body which was suspected as being the cause of the wheezing. He was a well-nourished baby, not very ill, and he had an audible wheeze on both inspiration and expiration; X-ray examination showed emphysema of the right lung. Bronchoscopic examination by Dr. R. V. Hennessy at this stage showed partial obstruction of the right main bronchus, probably from extrinsic pressure, together with a low-grade bronchitis. The Mantoux reaction was strongly positive, but culture of the fasting gastric content for tubercle bacilli yielded no growth. During the next three months he gradually lost his wheeze and cough, his temperature returned to normal and his appetite improved. During that time, for a period of ten weeks, he was given streptomycin, but it was impossible to assess whether the treatment hastened the disappearance of his symptoms. Several radiographs prepared during the period revealed an extraordinary chain of events in the right lung, the result of the bronchial lesion; first the upper lobe collapsed and then reexpanded, next the middle lobe collapsed and the lower lobe became emphysematous, and finally the lower lobe and middle lobe became completely collapsed with displacement of the mediastinum to the right side of the chest. From September, 1948, to July, 1949, he was at home and was fairly well, and had only a little spasmodic cough. Clinical and radiological examination showed collapsed lower and middle lobes of the right lung and right paratracheal glandular calcification. Bronchoscopy showed the right main bronchus occluded by watery granulation tissue immediately below the right upper lobe bronchus; a fine central slit in the granulation tissue allowed the passage of a catheter into the lower lobe, from which no less than 10 millilitres of creamy tuberculous pus were aspirated, this pus yielding a profuse growth of tubercle bacilli. Dr. Williams commented that that was a most astonishing finding, as the boy was well and had only a very slight cough. During the next two and a half years he steadily improved, had no symptoms, and steadily gained weight. Examination of the boy at the age of four years showed gross stenosis of the right main bronchus with, in the right lung, extremely shrunken bronchiectatic lower and middle lobes, a little calcification in the lung substance, and a normal but somewhat emphysematous upper lobe.

The third patient, D.A., illustrated the development of a stricture of the right main bronchus. In October, 1947, a healthy baby, aged four months, developed "bronchitis", her breathing being noisy and rattling. The cough and wheezing persisted for the next three months, but her general health, energy and growth were quite unaffected. In December, 1947, X-ray examination of the chest showed obstructive emphysema of the right lung and an enlarged right hilar shadow. Her Mantoux reaction was strongly positive, and on two occasions tubercle bacilli were grown from the fasting gastric contents. Bronchoscopy by Dr. R. V. Hennessy showed a narrowed right main bronchus immediately below the right upper lobe orifice and the bronchial mucosa was red and œdematous. On expiration the lumen of the right bronchus was reduced to a slit, but on inspiration it became patent again. From December, 1947, to April, 1948, the child continued to thrive, but the cough and wheezing in the chest persisted; during that time the middle lobe of the right lung collapsed, and later the upper lobe and then the lower lobe of the right lung. From May to August, 1948, a course of streptomycin by intramuscular injection was given without any appreciable effect either on the child's general condition or on the radiological appearance of the chest lesion. In September the right lung completely collapsed, but in December it reexpanded apart from the middle lobe, which remained collapsed. The middle lobe had now been persistently collapsed for over a year. Bronchoscopic examination on several occasions during 1950 showed a narrowing of the right main bronchus below the right upper lobe orifice, and that stenosis failed to dilate on passage of bougies. Several attempts at culture of the fasting gastric contents for tubercle bacilli failed to grow organisms. The child had no symptoms from the narrowing of the right main bronchus. A pneumonectomy was undertaken in August, 1950, as surgical opinion considered that the right lung was useless and a potential danger. An operative misadventure resulted in the child's death twelve hours after operation from asphyxia and shock due to retraction of the cut right bronchus. Post-mortem examination confirmed that death was due to asphyxia and shock, and the right lung was found to have a thickening of the medial wall of the right main bronchus from necrotic tuberculous granulation tissue in its wall, the thickening resulting in a narrowing of the lumen. The upper and lower lobes of the right lung were normal, and the middle lobe was collapsed with cylindrical bronchiectasis. There was no infection in the collapsed middle lobe. Examination of the hilar glands showed a little calcification in a few small shrunken necrotic glands.

Dr. Williams said that the three patients described illustrated clearly the natural history of the tuberculous hilar and mediastinal glands occluding or eroding the major bronchi, and setting up a series of events resulting finally in bronchiectasis. In the first patient pressure of the left upper lobe bronchus had resulted in lobar collapse and residual symptomless segmental bronchiectasis. In the second patient erosion of the right bronchus had resulted in granulation tissue causing collapse of the lower and middle lobes of the right lung with suppurating caseous pneumonitis; that partially healed, leaving gross bronchial stenosis and shrunken fibro-calcareo-caseous lower and middle lobes. In the third patient erosion of the bronchial wall by the tuberculous hilar glands had resulted in stricture of the right main bronchus and collapse of the middle lobe of the right lung with bronchiectasis.

Dr. Williams said that he had encountered 25 patients with bronchiectasis associated with a primary tuberculous lung infection. He had not followed the development of the bronchiectasis in all as closely as he had in the three patients described by frequent serial bronchoscopic examinations and bronchograms, but serial X-ray examinations and suitable bronchoscopic examinations and bronchograms revealed that the mechanism of the development of bronchiectasis was long-continued collapse or caseating pneumonia of a segment, lobe or whole lung, from occlusion or erosion of the bronchus by the tuberculous hilar glands or Ghon's focus. At times collapse and caseating pneumonia occurred together. When one considered the size to which the tuberculous glands grew in babies and children, it was surprising that bronchi escaped involvement as often as they did. The distribution of the affected lobes was widespread, and any lobe could be affected; in the one patient two or more lobes or segments could be involved. As it not infrequently happened that the primary tuberculous infection was entirely symptomless, so collapse of a lobe or segment could be symptomless, the patient being left with a bronchiectatic segment or lobe. There would appear to be very little doubt that that had been the course in Dr. Wait's patient, P.F., who was discovered with symptomless atelectatic bronchiectasis of the lower and middle lobes of the right lung.

Finally, two patients were shown, one of whom had developed pneumonia of the lower and middle lobes of the right lung, which failed to resolve; investigation showed stenosis of the right main bronchus, a positive Mantoux test result, a little calcification in the right hilar region, but a negative result from culture of gastric contents for tubercle bacilli. The patient, a girl, aged four years, had never been ill before, but there seemed to be very little doubt that she had had a silent tuberculous lung infection which had left stenosis of the right main bronchus. An accident in the form of bacterial pneumonia had occurred, and probably the bronchial stricture was an important factor in preventing resolution. The result had been suppurating pneumonitis with bronchiectasis necessitating surgical removal of the lower and middle lobes of the right lung by Dr. Russell Howard. It was eight months since the lung resection, and the patient had remained well.

The second patient, under the care of Dr. M. L. Powell, was a boy, aged six years, who had been found to have gross collapse, bronchiectasis and cavitation of the right lung. That state of affairs had been revealed only on routine physical examination during an attack of influenza, there being no symptoms, either pulmonary or general, to indicate the condition. The boy was an adopted child, but so far as his foster parents had been able to determine he had never been ill prior to adoption at the age of two years, and he had always been robust and healthy. His Mantoux reaction was positive, and tubercle bacilli were grown from his gastric contents. There seemed no doubt at the time that the boy had a gross tuberculous infection of his lung, and that the correct treatment was pneumonectomy, which was successfully carried out by Dr. Howard. However, at the time the answer was not forthcoming to the questions: How could such a lesion arise? How could such a lesion be symptomless? In the light of the experience with the other patients mentioned, there would seem to be little doubt that the boy had a silent primary tuberculous lung infection with ulceration of a gland into the right main bronchus. Collapse of the right lung followed, and then caseous pneumonia slowly and steadily destroyed the lung, leaving a shrunken, fibrotic, bronchiectatic, cavitated lung.

In discussing treatment, Dr. Williams said that the most important measure was to prevent tuberculous infection in children by detecting and controlling the infection in adults, as it was almost without exception that the adult infected the child. However, once an infant or child developed the primary tuberculous complex, very little could be done to prevent any complications from occurring. Streptomycin was of very doubtful value in the treatment of the primary complex and probably should be used only when tuberculous bronchopneumonia or hæmatogenous miliary dissemination occurred. It seemed very improbable that streptomycin could penetrate into the centre of a relatively avascular caseous gland with a high lipoid content. Some of the patients had been treated with streptomycin, and others had received no special treatment. As far as he could determine, Dr. Williams said, he could find no significant difference between the two groups. Furthermore he had had experience of three patients who actually developed collapse of a lobe whilst undergoing treatment with streptomycin for miliary dissemination.

Could aspiration by mechanical measures of caseous material, tuberculous pus or granulation tissue be of any value? Dr. Williams thought that it was of some value, but just how much was very difficult to say. Certainly it should be carried out if caseous material or granulation tissue was present.

Referring to surgical treatment, Dr. Williams said that resection of the bronchiectatic segment or lobe seemed to be indicated only when chronic pyogenic infection had occurred or when the diseased lung was the seat of a chronic tuberculous infection. As most of the patients were symptomless and well, surgical intervention would not seem necessary.

Dr. Williams said that his study indicated, firstly, that bronchiectasis was not one disease, but the end result of a number of different pathological processes of which primary tuberculous infection was one. Secondly, the true nature of bronchiectasis could often be understood only by closely following the evolution of the disease from its inception; without that knowledge it was often erroneous to give an opinion about the actual cause of the bronchiectasis in any one patient when it was encountered first in its fully developed state. Thirdly, most patients with bronchiectasis following primary tuberculous infection were symptomless and well and did not require treatment. Fourthly, if pyo-

genic infection occurred or the diseased lobe or segment was the seat of an active tuberculous lesion, then surgical resection was sound treatment.

In concluding, Dr. Williams said that his clinical investigation illustrated an important principle in clinical research, namely, that in certain disorders it was only by following the natural history of the disease from the early stages that the true nature could be revealed. The method was slow and tedious in diseases of a chronic nature.

DR. REGINALD WEBSTER said that all would be grateful to Dr. Williams for his clear and able demonstration of pathology in the living, as he had elucidated it by the coordinated application of bronchoscopy and radiography to the study of children suffering from a progressive primary tuberculous infection of the lung. The sequence of changes which Dr. Williams had traversed was in the majority of instances to be laid at the door of the lymph-nodal component of the primary complex, which was prone to involve a much greater extent of tissue than the primary focus itself, and to remain unresolved for an indefinite period after the initial lesion in the periphery of the lung had cicatrized. The facts elicited by Dr. Williams in his study of the children who provided the basis for his discussion indicated clearly that the point from which the bronchiectatic complication of pulmonary tuberculosis in childhood took origin was that at which bronchial occlusion had been established; such occlusion might ensue on the pressure exerted on the bronchus by an enlarged and caseating broncho-pulmonary lymph node, followed perhaps by the eruption of caseous matter into the lumen of a bronchus, with consequent endobronchial tuberculosis and aggravation of the bronchial stenosis by the intrusion into the lumen of tuberculous granulation tissue.

As Dr. Williams had indicated, the first of the sequelæ of bronchial stenosis or obstruction was emphysema in the lung field served by the affected bronchus—the so-called obstructive emphysema. Such emphysema was most strikingly manifest when its basis was a ball-valve obstruction incidental to the presence of a pedunculated and movable endobronchial tumour, or perhaps a foreign body. But an anatomical ball-valve mechanism was not essential to the production of obstructive emphysema, and it would seem that such an effect might be brought about by what he might term static stenosing agencies. Under normal conditions inspiration involved a high pressure difference for a relatively short period of time, and expiration a lower pressure difference acting over a longer period of time. That physiological fact might operate, in the presence of bronchial stenosis, in a similar (though less dramatic) manner to an actual ball-valve obstruction in the build-up of obstructive emphysema.

Dr. Webster said that as he understood the subject, the second stage in the march of events, should the bronchial stenosis advance to more or less complete occlusion, was collapse or atelectasis of a lobe or part of a lobe of the lung, according as the occlusion affected a major bronchus or one of the second or third order. With the occurrence of atelectasis the stage was set for the development of bronchiectasis, unless such atelectasis was a simple resorption phenomenon, brought about by pressure on the bronchus of an enlarged and contiguous lymph node, attended by no involvement of the bronchial wall in any specifically tuberculous process, and reversible with the reventilation of the lung which followed recession of the obturating lymph node. Unfortunately too often the process was far from being readily reversible, as when caseous material remained within the bronchial lumen as a plug, or when as the result of tuberculous infection of the bronchial mucous membrane, granulation tissue arose to encroach further upon the lumen of the bronchus.

Dr. Webster said that the vulnerability of an atelectatic pulmonary lobe or lobule to bronchiectatic changes was a matter of common recognition and suggested that it might be worth while to examine for a moment the steps by which bronchial dilatation supervened on atelectasis. This involved consideration of the changed mechanical equilibrium of collapsed pulmonary tissue. The atelectatic portion of lung was airless, and respiration effected no change in its volume —it had lost its plasticity and was relatively stiff. Under normal conditions the bronchus was embedded in air-filled, yielding pulmonary parenchyma, which took over the distension occasioned by inspiratory dilatation of the chest; the bronchus might be said to be cushioned against all but a small fraction of the pull of inspiration. If a bronchus was surrounded by atelectatic lung, then the stress and strain of the expanding chest were transmitted directly to the bronchial wall, the traction being unmitigated by the intervention of any yielding or accommodating medium.

The development of bronchiectasis in the evolution of a progressive primary complex might therefore be conceived as proceeding in the following manner. By diminution of the respiratory efficiency of a pulmonary lobe or lobule, the ability to get rid of secretion was impaired, and the affected lung suffered a depreciation, even a loss, of its self-cleansing power. Inadequate removal of physiological secretion of itself might lead to occlusion of small bronchi. When the interference with respiratory function was extreme, amounting to abolition, as in atelectasis induced by closure of the lumen of a larger bronchus, to retention of secretion were added loss of plasticity, stiffening and immobility of the collapsed lung, with consequent abnormal pull on the bronchial wall and ensuing expansion of the bronchus. The dilatation was at first reversible, but became permanent if the pathological processes contributing to its inception did not soon resolve. Eventually pyogenic infection supervened in bronchi abnormally dilated and clogged with secretion. Destruction of the bronchi followed, as the night the day, and with its advent the pathological state advanced beyond that of bronchial dilatation, or bronchiectasis, to a phase better described as bronchogenic suppuration. The bronchogenic abscesses which supervened on atelectasis as an episode in primary tuberculous infection of the lung were not necessarily tuberculous, and might well be due to pyogenic microorganisms. It had been argued with some force that the very immobility of a collapsed lobe served by a bronchus occluded by a tuberculous process rendered aspiration of infective tuberculous material improbable.

Dr. Webster concluded with a reference to experience in the cultivation of tubercle bacilli from material aspirated from bronchial lumina. He had notes of five children, in the course of the investigation of whom by Dr. Williams, *Mycobacterium tuberculosis* was cultivated from bronchial mucopus after repeated attempts to recover the organism from gastric content had failed. In a sixth child the reverse situation obtained, and a negative finding from the bronchial exudate was recorded at a date subsequent to the cultivation of tubercle bacilli from the gastric content. For a strict comparison of the utility of gastric content and bronchial mucus culture the two procedures should be synchronized as far as possible, and he was afraid that that had not always been the case. However, it was reasonable to expect that tubercle bacilli should be more susceptible of cultivation at the source of their discharge than at the end of a long migration and at the time of their imminent exit from the body.

DR. STANLEY WILLIAMS said that he was not sure that streptomycin was of little value in the treatment of enlarged caseous tuberculous glands which had ulcerated into the bronchial lumen. It was common knowledge that patients with a tuberculous ulceration of the larynx or bronchial tree responded very satisfactorily to the administration of streptomycin. He thought that when a tuberculous gland ulcerated into the bronchial tree, a similar state of affairs probably existed, and he considered that streptomycin would be of value in those cases. He also commented on the fact that it was unusual to find enlarged hilar or paratracheal lymph nodes pressing or ulcerated into the bronchial tree in children dying of tuberculous meningitis.

DR. L. P. WAIT wondered whether tuberculous arteritis occurred in the patients under discussion. He said that if it did it would be a possible factor in causing pulmonary changes from interference with the blood supply of the bronchi and might be indirectly responsible for causing bronchiectasis.

DR. JOHN PERRY said that in his experience in the post-mortem room, distortion of, compression of or ulceration of tuberculous glands into the bronchial tree was very unusual, but he fully realized that most of the patients whom he had examined *post mortem* had either died early in the disease or had had a long course of streptomycin. He further commented on the granulation tissue that was removed from some of the patients that Dr. Williams had shown and said that this tissue could not, on its own merits, be clearly defined as tuberculous tissue. He had no doubt that it was associated with a tuberculous process, as tubercle bacilli could be grown from bronchial mucus. He wondered whether the granulation tissue was not the result of pressure on the bronchus occurring immediately prior to ulceration of the gland into the bronchus.

DR. H. BOYD GRAHAM asked how common was tuberculous bronchiectasis. He had found that most children with well-developed bronchiectasis had "negative" Mantoux reactions. He also wondered whether enlarged hilar lymph nodes in pyogenic lung infection might not cause bronchial compression and collapse in a similar manner to that in which the enlarged tuberculous glands did so.

DR. RUSSELL HOWARD said that, concerning treatment, he had no doubt that if pyogenic infection occurred in one of the bronchiectatic lobes, or if there was an active tuberculous lesion discharging tubercle bacilli, then resection of the affected area was sound treatment. He did not agree with the opinion that patients with bronchial stenosis should be left until infection supervened. He thought that it was inevitable that, sooner or later, infection would occur, and then surgical treatment might be more difficult and more hazardous at that stage. He thought that resection could be undertaken safely in all patients with bronchial stenosis uncomplicated by pyogenic infection.

Successful Colectomy for an Irreducible Intussusception.

DR. J. G. WHITAKER showed a patient, aged six months, who had presented at the hospital with an intussusception of four days' duration, and on whom he had carried out successfully a resection of gangrenous gut. The baby was a healthy child, who had not been ill until four days before her admission to hospital on April 27, 1951. She had had spasms of crying and had refused feedings for four days; the day before her admission to hospital she had passed blood on several occasions by the bowel. There had been no stools passed for three days, and during that time she had vomited. Examination showed her to be a very shocked, pale, dehydrated child, with a temperature of 106° F., a pulse rate of 140 per minute, and a respiration rate of 26 per minute. The abdomen was distended, and a cylindrical mass was felt in the upper part of the abdomen; the mass extended down the left side of the abdomen.

There was little clinical doubt that the child had an intussusception of four days' duration and was in a state of moderate circulatory collapse. The shocked state was treated with a transfusion of three ounces of blood, together with an intravenous infusion of 5% glucose solution in normal saline. The alimentary tract above the obstruction was aspirated by passing a tube into the stomach. Operative treatment was carried out five hours after this treatment was commenced, when the child presented a reasonable operative risk. Anæsthesia was commenced with cyclopropane and curare and ether, and the abdomen was opened with a right paramedian incision. An intussusception which was irreducible was found, the intussusception being of the ileo-colic type and also colo-colic with rupture of the ensheathing layer and protrusion of the apex of the intussusception into the peritoneal cavity. At that stage the child became very collapsed, and there was considerable doubt about whether she was still living. A further ten ounces of blood were given, and that made possible rapid excision of the terminal six inches of the ileum, the caecum, and the ascending, transverse and descending parts of the colon; then a side-to-side anastomosis of the ileum and sigmoid colon was carried out. The abdomen was closed in layers without drainage.

Dr. Whitaker said that considering the extent of the surgical procedure, the child's post-operative course was amazingly smooth and uneventful. Water, glucose, sodium, chloride, potassium and serum were given in appropriate amounts intravenously, and oral feedings were commenced on the third day after operation. There was no vomiting or abdominal distension at any stage, and the bowels began to act the day after operation. The number of bowel motions increased rapidly, so that by the fifth day the child was passing as many as fourteen motions per day; but after that the number rapidly decreased, until after a period of two weeks she was passing only three to four normal motions per day. The wound healed well, and the baby commenced to gain weight. When last examined two months after operation the baby was gaining weight at the rate of nine ounces per week.

Dr. Whitaker, in summing up the case, said that the infant's recovery was a triumph for teamwork. Without skilled pre-operative and post-operative intravenous therapy, which had been ably conducted by Dr. Aberdeen, and without skilled anæsthesia, which had been carried out by Dr. McDonald and Dr. Stanton, the surgeon's skill would have been useless. As far as he knew it was the most extensive bowel resection that had been carried out for an irreducible intussusception in the Children's Hospital. He said that the key to the problem of irreducible intussusception should lie in its prevention, and that was one aspect of teaching that was very important for the undergraduate who was training to become a family doctor. He stressed the value of giving an anæsthetic to a child suspected of having an intussusception, for it was only by that means that satisfactory palpation of the abdomen could be carried out. If the surgeon was faced with an irreducible intussusception, Dr. Whitaker thought that in most cases an ileo-colostomy with exteriorization of the damaged bowel was the safest and most satisfactory procedure.

DR. MURRAY CLARKE emphasized that the case just discussed was most unusual, both in the operative findings and in the happy surgical outcome. It showed, he said, that it was necessary to get away from pre-war ideas and to realize that with adequate chemotherapy and supportive treatment to adjust electrolytic and fluid balance, they had embarked on a new era in pædiatric abdominal surgery. But resection was still a necessity to be dreaded. Australian figures for intussusception were good, primarily because the general practitioner was so aware of the condition that the patient usually reached the surgeon early. Dr. Clarke said that the problem of the surgeon was the very ill patient with a long history and with an intussusception which would not reduce. Should the surgeon attempt a very difficult reduction which might be unsuccessful and leave a badly shocked patient, or should he carry out a resection? That was a very difficult decision to make in some cases. Resection was indicated by irreducibility and by perforated or non-viable gut. Dr. Clarke referred to a recent successful resection in a child of fifteen months whose obstruction from intussusception had reached the late stage of copious fæcal vomiting, ladder pattern and multiple fluid levels in a plain X-ray picture. A resection with side-to-side anastomosis was performed, but he suggested that convalescence might have been quicker if a closed aseptic Mikulicz resection, in which the layers of the abdominal wall were closed before the damaged bowel was cut off, had been adopted. It was very gratifying to see the extraordinarily good figures relating to mortality in those cases in which in recent years resection had been required at the Children's Hospital, but even better results would follow wider use of that operation, which was speedy and avoided soiling of the peritoneum.

DR. J. BEGG referred to a case in which gut of doubtful viability had been returned to the peritoneal cavity with subsequent perforation and the formation of a huge abscess, which was drained. A considerable area of bowel sloughed and the patient's condition rapidly deteriorated while the ileostomy was draining, but it was possible later to perform a side-to-side anastomosis and to close the fistula. Dr. Begg stressed the importance of performing resection of severely damaged gut. In the ileo-ileal type of intussusception, if resection was necessary, it was technically very difficult to anastomose normal ileum to swollen œdematous terminal ileum, and in that type of case an ileo-transverse colostomy was the procedure of choice.

DR. B. R. HALLOWS discussed four points of operative technique which he had found of value in the treatment of intussusception in the late stages. The first was deliberate section of returning and ensheathing layers. During attempted reduction the ascending colon was split in the longitudinal axis, and the two layers mentioned were deliberately incised to continue in line with the rent. That enabled the intussusception to be reduced readily, and the gut examined, the gangrenous portion, if any, removed, and anastomosis completed. The second point was section of the ensheathing layer and the application of digital pressure to the apex of the intussusception. That procedure was of great value if the terminal inch was irreducible. If no resection was necessary, the rent in the ensheathing layer was sutured. The third point was the Mikulicz-Paul type of resection, a proximal and distal anastomosis being performed at the same time; thus the exteriorized portion of the gut was by-passed. The final closure was carried out at a later stage. The final point was the application of hot packs and gentle even pressure to the mass, and at the same time gentle traction on the entering portion. That manœuvre facilitated the reduction of the final inch or so of the intussusception.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held in the Anatomy Lecture Theatre, Frome Road, Adelaide, on June 1, 1951.

Transmissible Disease and Population Control in Some Wild Animal Populations.

DR. J. A. R. MILES gave an account of some of the investigations of the mechanisms of population control among rodents. He said that, despite numerous investigations designed to show the relation of transmissible disease to

the rapid fall which regularly ended the peak period in the numbers of those rodents liable to cyclical variation, there were very few occasions on which such disease had been clearly shown to be the main factor. The well-known case of plague in the rat stood almost alone, although a toxoplasm had some claim to be regarded as the cause of a crash in the numbers of the field vole (*Microtus agrestis*) in the United Kingdom on one occasion. In Northern Canada and parts of the Union of Socialist Soviet Republics a great increase in the numbers of predators might be responsible for a rapid fall in numbers, but in the thickly populated civilized areas of Western Europe no adequate rise in the numbers of predators was possible. An interesting observation, the significance of which had not yet been evaluated, was that concerning "shock disease" of hares described by Larson and Bell. They found that during the period of the crash in numbers after the peak of a hare cycle in the middle west of the United States of America, hares which could usually be kept in captivity without difficulty, would after a short period in captivity go into convulsions followed by coma and death. Such convulsions were due to acute hypoglycæmia and could be temporarily cured by intravenous injection of glucose, but would always recur later. The causation of the syndrome was not certain, but further work on it had been started in the United States of America and it was hoped that Larson and Bell would be able to give more information during the next few years.

Dr. Miles went on to say that the study of population control in birds had not received so much attention as that in rodents, but one of the most thorough investigations of a wild animal ever made had been that made by the Grouse Committee in Great Britain and published in "The Grouse in Health and in Disease" in 1911. That work clearly showed that under the somewhat artificial conditions existing on grouse moors in Great Britain, a transmissible disease due to the nematode *Trichostrongylus pergracilis* was the main limiting factor to the population of red grouse (*Lagopus scoticus*). Recent investigations by Surry-Dane, Stoker and Miles had shown that there had occurred for at least five years a very severe epizootic among juvenile manx-shearwaters (*Puffinus puffinus*) on one of their main breeding stations. That disease was probably killing at least 75% of the juvenile birds in the areas most severely affected, but it had not been possible to show conclusively that there had been any diminution in the number of breeding birds in the area. That might be partly accounted for by the longevity of adult shearwaters, which did not appear to be affected by the disease, and partly by immigration of breeding birds from other areas. Recently the fulmars (*Fulmarus glacialis*) on the Faroe Islands had developed psittacosis, and the occurrence of the disease in the birds had been discovered by Rasmussen because of the occurrence of the disease in annual human epidemics when the young fulmars were taken for food. The disease later spread to Iceland. Miles and Shrivastav had shown that the rate of infection among Faroese fulmars had increased during the last ten years. Despite the advent of the disease the fulmars were still rapidly increasing in numbers, helped in part by the cessation of human exploitation because of the high rate of disease among the wives of the fowlers.

Dr. Miles said, in conclusion, that the information about the subject was extremely patchy and inadequate, but it was at least clear that transmissible disease was only one among a large number of factors involved in population control, and that it was certainly far less important than either man's direct intervention for his own welfare or his indirect intervention through alterations to habitats.

Correspondence.

PHARMACEUTICAL BENEFITS ACT.

SIR: Following a letter from Dr. E. H. White in THE MEDICAL JOURNAL OF AUSTRALIA of July 14, 1951, I would like to make the following comments:

1. We must, as I have said before, in a letter to your journal last year, congratulate Sir Earle Page on his masterly effort in succeeding in coming to agreement with the British Medical Association and giving the public life-saving drugs, and Pensioner Medical Service medical and drug benefits, when previous governments were totally unable to bring down a scheme and get it into operation.

2. Prescribing is not always easy, but with a little patience, and occasionally reference to a local chemist, most difficulties disappear.

3. I imagine there will certainly be adjustments to the list, and alterations from time to time to meet altering situations, but fundamentally we should be prepared to admit there has been a definite advance made in the direction of meeting the public need, and with a minimum of inconvenience to the practising profession.

4. With the rising spiral of inflation, we may well find that this section of the Government's health scheme has not arrived a moment too soon, and may be the means of preserving that part of private medical practice which might otherwise have been permanently lost to the profession, and there may have been no alternative to a socialized profession, as we have seen to our sorrow in Great Britain and New Zealand.

5. In conclusion, sir, may I suggest that our best form of criticism should be of a constructive nature, and be directed towards amplifying the scheme already in action, and, if possible, in broadening the operation of the act, so that the most deserving section of the general public are well covered, whilst those best able to look after themselves are not given government aid which they do not require.

Yours, etc.,

H. T. ILLINGWORTH.

Kalgoorlie,
Western Australia,
July 18, 1951.

THE GUILLAIN-BARRÉ SYNDROME: THREE CASES IN ABORIGINAL NATIVES.

SIR: I read with interest the article by Dr. Eric Saint on the Guillain-Barré syndrome in your issue of July 14, 1951. He states that there is no specific cure for this syndrome. I agree, but wish to draw his attention to an article appearing in *The Journal of the American Medical Association*, May 20, 1950, by Nicholas E. Creatvro, M.D., in which he treated cases of the Guillain-Barré syndrome with dimercaptopropanol (BAL), giving 1·5 milligrammes per kilogram of body weight intramuscularly. He reports excellent results.

Yours, etc.,

MICHAEL ELYAN, D.C.H.,
Pædiatrician, Townsville Hospital.

Townsville,
Queensland,
July 19, 1951.

Post-Graduate Work.

LECTURE BY PROFESSOR GORDON MURRAY.

The Post-Graduate Committee in Medicine in the University of Sydney, in conjunction with the Royal Australasian College of Surgeons, wishes to announce that Professor Gordon Murray will lecture in the Stawell Hall, 145 Macquarie Street, Sydney, at 8.15 p.m. on Wednesday, August 22, 1951. His subject will be "Vascular Surgery".

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 50, of July 12, 1951.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH.

Royal Australian Naval Reserve.

Appointments.—Lindsay Henry Jones is appointed Surgeon Lieutenant, dated 27th April, 1951. Rex Justice John Gray and Robert Spencer Packard are appointed Surgeon Lieutenants, dated 2nd May, 1951.

Royal Australian Naval Volunteer Reserve.

Promotion.—Surgeon Lieutenant Francis Callum Archibald is promoted to the rank of Surgeon Lieutenant-Commander, dated 22nd January, 1951.

AUSTRALIAN MILITARY FORCES.

Royal Australian Army Medical Corps.

3/37652 Lieutenant-Colonel W. D. Refshauge, O.B.E., is transferred from the Citizen Military Forces, is appointed Deputy Director-General of Medical Services, and to be Colonel, 1st May, 1951.

NX700269 Honorary Captain M. J. Deakin is appointed from the Reserve of Officers, and to be Captain, 30th April, 1951.

To be Captain, 2nd April, 1951.—3/40053 Donald Headley.

To be Temporary Major, 5th April, 1951.—VX700107 Captain G. W. Cooper.

Citizen Military Forces.

Northern Command: First Military District.

Royal Australian Army Medical Corps (Medical): To be Captain (provisionally), 23rd April, 1951.—1/39109 Gerard Joseph McCafferty.

Southern Command: Third Military District.

Royal Australian Army Medical Corps (Medical).—3/101001 Lieutenant-Colonel W. D. Refshauge, O.B.E., relinquishes command 4th Field Ambulance and is transferred to the Interim Army, 1st May, 1951. To be Captain (provisionally), 23rd April, 1951: 3/101016 Robert David Wilson.

Central Command: Fourth Military District.

Royal Australian Army Medical Corps (Medical).—4/35233 Major J. D. Rice is appointed from the Reserve of Officers and is borne supernumerary to the authorized establishment of Majors with pay and allowances of Captain (at his own request), 4th April, 1951.

Western Command: Fifth Military District.

Royal Australian Army Medical Corps (Medical).—5/32063 Major W. P. White, E.D., is appointed from the Reserve of Officers, 1st April, 1951.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

1st Military District: To be Honorary Captain, 2nd May, 1951.—Arthur Lawrence Proctor.

2nd Military District.—The resignation of Captain B. E. Frecker of his commission is accepted, 15th August, 1950.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force: Medical Branch.

Squadron Leader C. W. Fitton (033030) is appointed to a permanent commission, 26th February, 1951.

The probationary appointment of the following Flight Lieutenants is confirmed: R. G. Sharp (023027), B. N. Turner (023026), J. F. Howell-Price (023025), B. Capper (023023), W. C. Gadd (04592), G. J. Fowler (023038).

The following are appointed to short-service commissions, on probation for a period of twelve months, with the ranks indicated: (Flight Lieutenants) Desmond Joseph Hannan (012786), Francis Ian Walke (012787), 26th April, 1951; (Pilot Officer) Donald Bruce McKillop (024158), 30th April, 1951.

The resignation of Flight Lieutenant B. Capper (023023) is accepted, 30th May, 1951.

Notice.

THE ARTHUR WILSON MEMORIAL FUND.

THE following donations have been received for the Arthur Wilson Memorial Fund, which will be devoted to research into problems of childbirth; they are acknowledged with thanks. Donations may be sent to Dr. C. K. Churches, honorary treasurer, 122 Flinders Street, Melbourne, C.1, and will be acknowledged in this journal. Previously acknowledged £2108 12s., Dr. R. S. Smibert £20, Dr. Ian Stahle £15 15s., Dr. Bernard McColl £12 12s., Dr. I. J. Paull £10 10s., Dr. W. McLaren £10 10s., Dr. and Mrs. Robert Southby £10 10s., Dr. John Colebatch £5 5s., Dr. R. Douglas Aitchison £3 3s., Dr. Arthur Joyce £3 3s., Dr. and Mrs. Clifford Rosefield £3 3s., Dr. Lucy Bryce £2 2s. Total £2205 5s.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JULY 21, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	*	..	1	..	..	..	..	..	1
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	5(5)	1	..	..	..	..	..	..	6
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	5(5)	..	..	..	..	..	5
Diphtheria	4(4)	6(5)	2(1)	1	6(4)	..	..	..	19
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	6(6)	..	..	..	..	..	..	6
Encephalitis Lethargica	..	2(2)	..	..	..	..	..	..	2
Erysipelas	*	*	*	..	*	*	..	..	..
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	..	..	*	*	*	*	..
Lead Poisoning	..	..	..	*	*	*	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	1(1)	*	..	1	..	..	..	2
Measles	*	*	..	75(36)	*	*	..	..	75
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	33(12)	14(3)	29(14)	23(16)	5(3)	..	..	..	104
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	1	..	..	..	..	..	1
Rubella(*c*)	*	*	*	*	..	*	..	..	..
Scarlet Fever	11(7)	16(12)	2	5(3)	2(2)	1(1)	..	..	37
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	..	*	*	*	*	*	..
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	30(25)	46(38)	22(11)	5(4)	15(11)	6(2)	..	..	124
Typhoid Fever(*e*)	..	..	2(2)	..	..	..	..	..	2
Typhus (Endemic)(*f*)	..	..	2	..	3(1)	..	..	..	5
Undulant Fever	..	..	..	..	1(1)	..	..	..	1
Weil's Disease(*g*)	*	*	..	*	*	*	*	*	..
Whooping Cough	*	*	*	3(2)	*	*	..	..	3
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory.
* Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Obituary.

GEORGE MESTON DUNCAN.

WE regret to announce the death of Dr. George Meston Duncan, which occurred on August 1, 1951, at Gosford.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Bowring, Aubrey Charles, M.B., B.S., 1948 (Univ. Sydney), Milton Hall, 93 Milton Street, Ashfield.
Ivanov, Aksel, M.B., B.S., 1951 (Univ. Sydney), 17 Blandford Avenue, Waverley.
Nield, James Marland, M.B., B.S., 1951 (Univ. Sydney), Balmain and District Hospital, Balmain.
Pitsch, Werner Jobst, M.B., B.S., 1951 (Univ. Sydney), 9 Rosetta Avenue, Killara.

The undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Richards, Eric Dean, M.B., B.S., 1951 (Univ. Adelaide), Leigh Creek, South Australia.
Jackson, John Frederick, M.B., B.S., B.Sc., 1951 (Univ. Adelaide), 12 Bartley Crescent, Wayville.

The undermentioned have been elected members of the South Australian Branch of the British Medical Association:

Kneebone, Clive Stuart, M.B., B.S., 1951 (Univ. Adelaide), 62 Anzac Highway, Everard Park.
Vivian, Arthur Brian, M.B., B.S., 1951 (Univ. Adelaide), "Benacre", Glen Osmond Road, Glen Osmond.

Medical Appointments.

Dr. N. S. Harbison has been appointed public vaccinator for the Shire of Numurkah, Victoria.

Dr. C. Checchi has been appointed public vaccinator for the Shire of Ararat, Victoria.

Dr. B. J. Doran has been appointed public vaccinator for the Shire of Gisborne, Victoria.

Dr. A. T. Taylor has been appointed public vaccinator for the Shire of Mornington, Victoria.

Dr. G. R. Jones has been appointed public vaccinator for the Shire of Swan Hill, Victoria.

Dr. W. H. G. Steele has been appointed public vaccinator for the Shire of Castlemaine, Victoria.

Dr. R. M. Ford has been appointed medical superintendent of the Morris Hospital, Northfield, South Australia.

Dr. L. J. Dunstone has been appointed deputy superintendent of the Enfield Receiving House, Enfield, South Australia.

Dr. J. E. Cawte has been appointed deputy superintendent of the Northfield Mental Hospital, Northfield, South Australia.

Dr. W. E. King has been appointed a member of the Dental Board of Victoria.

Dr. J. W. Rollison, Dr. G. H. Burnell and Dr. L. R. Mallen have been appointed members of the Nurses Board of South Australia.

Dr. H. J. Ellis has been appointed honorary assistant anæsthetist at the Royal Adelaide Hospital.

Dr. W. Christie has been appointed principal medical officer for schools in the Department of Public Health, South Australia.

Dr. Naomi Rosslyn Ryan, Dr. Eleanor Marcella Sexton and Dr. Marjorie Phyllis Casley Smith have been appointed medical officers in the Department of Public Health, South Australia.

Dr. H. G. Wallace has been appointed a member of the Dental Board of New South Wales.

Dr. M. M. Poulter has been appointed a government nominee on the Board of the Devonport Public Hospitals District, Tasmania.

Dr. S. C. Milazzo has been appointed medical registrar at the Royal Adelaide Hospital.

Dr. J. A. Earl has been appointed pathological registrar at the Royal Adelaide Hospital.

Dr. R. R. Margarey, Dr. A. G. A. Tregonning, Dr. J. A. M. Walker and Dr. J. G. Durham have been appointed associate medical officers of the Royal Adelaide Hospital.

Dr. A. E. Lincoln has been appointed public vaccinator for the Shire of Newham and Woodend, Victoria.

Dr. A. R. Steel has been appointed public vaccinator for the Shire of Bright, Victoria.

Dr. J. I. de Boer Leembruggen has been appointed public vaccinator for the Shire of Gordon, Victoria.

Dr. L. Willson has been appointed government medical officer at Hughenden, Queensland.

Diary for the Month.

AUG. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
AUG. 22.—Victorian Branch, B.M.A.: Council Meeting.
AUG. 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
AUG. 24.—Queensland Branch, B.M.A.: Council Meeting.
AUG. 28.—New South Wales Branch, B.M.A.: Ethics Committee.
AUG. 30.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

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